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14. ABSTRACT
The purpose of this project is to conduct DoD high priority research in: vascular injury, pain, and airway management. These studies will extend evidenced-based pre-hospital interventions as well as populate the National Trauma Research Repository (NTRR). During the initial year, subcontracts have been issued, IRB approvals were secured. One study has HRPO approval and is enrolling subjects and the other is pending HRPO approval. The trauma repository and airway simulator projects are on schedule. There are no major finding or results at this time.

15. SUBJECT TERMS Vascular injury, airway management, pain management, Ketamine, National Trauma Research Repository, research dissemination

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INTRODUCTION:

Advances in trauma care in both pre-hospital and hospital settings have reduced trauma-related deaths and morbidities markedly; however, there is a substantial opportunity to further reduce deaths in the pre-hospital setting. Gaps in civilian and military pre-hospital care must be closed in order to reduce the number of potentially preventable deaths among Wounded Warriors and civilian trauma patients. The purpose of this project is to focus on three specific areas of research identified by the DoD as high priority including: better solutions for vascular injuries, improved pain management, and better approaches for airway management. These studies will extend evidenced-based pre-hospital interventions as well as populate the National Trauma Research Repository (NTRR) that will allow for data sharing, secondary analysis and greater power to detect statistical significance. As available research funding shrinks and federal budget pressure increases, it is essential that the return from dollars invested in research be maximized by replacing the expensive and repetitive assembly and disassembly of short-lived clinical investigator networks with a stable and enduring operational infrastructure for clinical trauma research.

KEYWORDS:

Vascular injury, airway management, pain management, Ketamine, National Trauma Research Repository, research dissemination

ACCOMPLISHMENTS:

Major Objectives of the Project:

Objective: To conduct research projects addressing military research gaps in airway management, pain management and vascular injury; and to develop tools to allow for the collection and dissemination of results and data from studies

Technical Objective 1: To conduct research projects addressing military research gaps in airway management, pain management and vascular injury**;** the contractor will perform Award management and compliance to include subcontracts, contract compliance, and all appropriate USAMRMC HRPO requirements.

Technical Objective 2: To develop tools to allow for the collection and dissemination of results and data from studies, including:

1) Develop a scalable repository of translational research data.
   a) Determination of common data element based on previously NTI funded project and other database sources.
   b) Creation of the data dictionary
   c) Development of policies for utilization guidance which includes repository requirement documents and website development.
   d) Conduct vendor solicitation and vendor selection process based upon requirements and capabilities identified.
   e) Build a scalable repository
   f) Alpha and beta testing with previous NTI funded studies and studies funded through this cooperative agreement.

2) Provide a forum for dissemination of research outcomes to the trauma community.

Accomplishments under these Goals:

Major activities of this grant are organized under two study protocols and two projects.

STUDY 1:
Protocol Title: Determining the Efficacy and Safety of Ketamine as a Battlefield Analgesic
Principal Investigator: John Fauerbach, PhD
Participating Site: Johns Hopkins University School of Medicine
HRPO Assigned A-number: Pending
Abstract: Background: Early, effective pain control for acute traumatic injury is important for successful outcomes. Despite the known importance of pre-hospital pain management, few studies have reported the use of analgesics and the type of analgesics used in combat. Ketamine has emerged recently as a potentially effective analgesic alternative to narcotics for use in combat-associated casualties. While early case reports attest to its effectiveness, these reports are anecdotal. Ketamine is the only single-agent anesthetic capable of producing a "dissociative" anesthesia, which has been useful for a variety of outpatient and inpatient surgical procedures. More than 50,000 service members have been injured in OIF, OEF, and OND and experience varying degrees of pain throughout their care. Of these injured service members, 31.8% are also diagnosed with PTSD.
Hypothesis: The addition of ketamine to narcotic analgesics will reduce significantly self-rated pain during dressing change/debridement on the Visual Analogue Scale for Pain (VAS-Pain):
Methods: Persons enrolled in the study through the informed consent process will be patients admitted to the Johns Hopkins Burn Center after sustaining burns less than 25% total burn surface area and not requiring initial endotracheal intubation. This would enable them to participate in structured interviews conducted by a psychologist assigned to the Burn Unit. These interviews would evaluate:
• The effectiveness of sub-anesthetic doses of ketamine as a sole analgesic vs. as a narcotic sparing drug for the treatment of acute post-traumatic pain
• The side effect profile of ketamine when administered in sub-anesthetic doses
• Whether the early administration of ketamine during the first three days following injury has a sustained effect on reducing the incidence or severity of Post-Traumatic Stress Disorder (PTSD)
• Whether the early administration of ketamine during the first three days following injury has a sustained effect on reducing the incidence or severity of clinical depression

Once IRB and HRPO approval is secured, patients will be randomized to a trial comparing a usual pain regimen, typically narcotics and benzodiazepines (UR-N) against a low dose ketamine regimen supplemented with usual pain medications (K+UR) on the effect of self-reported pain severity at the start of the procedure, every 5 minutes during the procedure and 5 minutes after the procedure ending, as well as the incidence and severity of PTSD and Depression at 24 hours, one week, and one month.

Military Significance: The DOD has identified capability gaps in combat casualty care. Several of the high priority gaps are well-suited for research in the civilian setting including en route care. A specific gap in these capabilities that the DoD has identified as high risk to the military and amenable to study in the civilian setting is: Ability to provide 100% acute and chronic pain management for wounded and injured soldiers, starting at the point of injury and continuing across the spectrum of care.

Progress Reported:

Refinement of eligibility criteria and exclusion criteria as well as drafting of the screening protocol, enrollment protocol and final consent form was accomplished as stated in the Scope of Work. The human subjects documentation (study protocol, consent form, etc.) was submitted to the local IRB and is pending approval by the High Risk Review Committee. That committee has asked for minor clarification regarding the role of nurses on the protocol. This study is seeking authorization to screen 300 for 100 completers. Enrollment targets will be adjusted in Year 2 so that the total project enrollment goal will be reached (100 completers).

The PI, Dr. Fauerbach, is working with the John Hopkins Bayview Medical Center pharmacy to finalize drug handling procedures such as clarify procedures for sub-anesthetic, low-dose, slow infusion of ketamine for pain management during wound care sessions. The participant recruitment folder has been completed and the protocol Manual of Operations is in final stages of preparation. Study clinical report forms are in the final stage of completion. The research team is under development. The core/faculty members are in place. The selected study coordinator cannot be hired until funds have been freed by School of Medicine. This is dependent upon the above-mentioned IRB and DoD final reviews/approval.

The Study 1 team presented a poster depicting the protocol for the "Ketamine for Acute Burn Pain" project at a local Behavioral Pharmacology Research Unit conference (Appendix A).

Study 1: Participant Accrual in Year 1

Site	Recruited	Screened	Enrolled	Completed
Johns Hopkins University	0	0	0	0

Number of subjects recruited/original planned target: **0/300**
Number of subjects screened/original planned target: **0/300**
Number of patients enrolled/original planned target: **0/100**
Number of patients completed/original planned target: **0/100**

STUDY 2

Protocol Title: The PROspective Observational Vascular Injury Trial (PROOVIT)
Principal Investigator: Joseph DuBose, MD (Travis Air Force Base)
Lead Site: University of California at Davis
Participating Sites: Baylor College of Medicine/Ben Taub Hospital, Emory University, Loma Linda Medical Center, University of Southern California, Scripps Health, University of Maryland/R. Adams Cowley Shock Trauma, University of Tennessee – Memphis, University of Texas Health Science Center at Houston, University of Wisconsin School of Medicine and Public Health, Wright State University, University of Texas Health Science Center at San Antonio
HRPO Assigned A-number: A-19299.1a-1i
Abstract: Background: Few if any decisions throughout the phases of vascular trauma management are guided by strong evidence. This fact is unfortunate, as many new diagnostic, therapeutic and surveillance strategies have the potential to improve morbidity and mortality following this vexing injury pattern. The lack of evidence-based practice is even more concerning given the devastating consequences associated with mismanaged vascular trauma.

To date, no studies exist that would allow the prospective aggregation of larger amounts of data pertaining to all phases of vascular trauma management.
Hypothesis: This prospective, multicenter, observational study will provide the necessary data to develop best practices and optimize the care of this unique population of patients.
Specific Aims: 1. To determine the impact of tourniquet utilization after extremity vascular injury on limb-specific complications and limb salvage; 2. To determine the optimal utilization of endovascular versus open repair modalities after vascular injury; 3. To determine the role of early anticoagulation in mitigating complications after vascular injury repair.
Study Design: This study is a prospective multi-center observational trial on the management of vascular trauma. Data and endpoints will be observational and involve no proscribed therapeutic interventions or alterations in patient care. Waiver of informed consent has been received. Institutions and providers are conducting normal diagnosis, management and surveillance procedures without interference by this study. The location and type of endovascular therapy for vascular trauma is tracked including comparison of outcomes to those following open operative repair of similar injury patterns. Finally, data elements are gathered in a wide range of age groups with vascular trauma including the challenging scenarios of pediatric and geriatric vascular injury.
Military Benefit: Hemorrhage from vascular injury, at both Non-Compressible Vascular Injury (NCVI) and Compressible Vascular Injury (CVI) sites, remains a primary cause of mortality and morbidity on modern battlefields. This study will provide linkage to crucial elements of subsequent limb salvage and long term outcomes – data that are presently not available on any significant scale in the military realm.

Progress Reported:

This study is a prospective multi-center observational trial on the management of vascular trauma. Data and endpoints are observational and involve no proscribed therapeutic interventions or alterations in patient care. The location and type of endovascular therapy for vascular trauma will be tracked including comparison of outcomes to those following open operative repair of similar injury patterns.

In the first year of this project, the PROOVIT study was adapted to current funding status. All subawards were executed. All clinical sites had existing IRB approval or received timely continuing review and approval from HRPO. Clinical sites are screening and enrolling. (The University of Texas Health Science Center at San Antonio (UTHSCSA) is providing statistical analysis only). PROOVIT has enrolled 561/5,000. The projected enrollment for the first year was 250 subjects, therefore, this study is well-ahead of the timeline set forth in the scope of work.

Study 2: Participant Accrual in Year 1

Site	Recruited	Screened	Enrolled	Completed
Baylor	85	85	85	14
Emory	50	50	30	20
HSC-Tennessee	121	121	40	40
Loma Linda	157	157	90	90
Scripps	55	55	6	0
UC Davis	32	32	22	10
University of MD	4,055	4,055	84	16
USC	21	21	21	0
UT Houston	194	194	87	0
Wisconsin	0	0	0	0
Wright State	141	141	108	108
Total	4,911	4,911	573	298

Number of subjects recruited/original planned target: **4,911/5,000**
Number of subjects screened/original planned target: **4,911/5,000**
Number of patients enrolled/original planned target: **573/5,000**
Number of patients completed/original planned target: **298/5,000**

PROJECT 1

Project Title: High Anatomic Fidelity Surgical Airway Training System
Principal Investigator: Robert Buckman, MD
Lead Site: Operative Experience, Inc.
HRPO Assigned A-number: Not applicable

Abstract: Background: Airway obstruction is the third most common cause of potentially-preventable combat death. Because of this, surgical management of the threatened or obstructed airway is an essential skill for special operations medics and combat surgeons. Cricothyroidostomy and tracheostomy are infrequently performed, life-saving surgical procedures required when a casualty's airway cannot be maintained by other means. Surgical airway procedures may be required at any level along the continuum of care/evacuation. Published data from recent theaters of war indicate that these emergency procedures are often performed incorrectly. Due to the limitations of existing methods of training, surgical airway management procedures are not currently taught to all combat medics. Improved, simulation-based methods of training will not only improve the training and enhance the capability of SOF medics and surgeons, but also will allow additional military healthcare providers and even combat lifesavers to be trained in this critical skill. The Defense Health Board recommended optimized airway devices and training as a research priority for the Combat Casualty Care Research Program, contributing to the identification of a Combat Casualty Care Capability Gap. Methods: Develop a prototype surgical airway simulator that provides high anatomical and surgical fidelity and challenges trainees with increasing degrees of clinical difficulty.

This project will develop an airway simulator that is capable of accurate anatomic representation of the airway from the mouth to the lungs, simulates a variety of traumatic tissue disruption with the face and neck, bleeds realistically, and supports training in tracheostomy and cricothyroidotomy. Development includes anatomic design, engineering design, medical modeling, physical modeling, engineering and system integration.

Progress Reported:

The subcontract was fully executed on 05/12/2016. The PI and Operative Experiences, Inc. (OEI) completely developed the model base and integrated electro-mechanical systems. Programmable logic controllers (PLC) have been developed, but have not yet been fully integrated. OEI has substituted a microcontroller to support more hardware at lower cost. Programming is underway with new applications. Appendix B presents photographs of the model under development.

PROJECT 2

Project Title: National Trauma Research Repository
Principal Investigator: Donald Jenkins, MD
Lead Site: The National Trauma Institute
HRPO Assigned A-number: Not applicable
Abstract: There is a critical need for a national trauma research repository to synthesize study data for maximum use. Advances due to clinical trauma research have been accomplished largely through separate, organizationally distinct and disconnected efforts. Even when funding has derived from federal entities, individual projects have been somewhat dispersed and uncoordinated. This situation leads to research delays, duplications, inefficiencies and increased costs. To date there relatively little attention has focused on data exchange in the clinical research domain. While clinical researchers in different locations may have similar lines of investigation, the computer systems in use to store and retrieve data locally do not, and for the most part cannot, transmit, receive, combine, analyze and use shared data as information. Clinical research data are fragmented, sometimes within one facility, and can rarely be repurposed to answer additional research questions. Sharing data maximizes its value, promotes follow-up studies and minimizes duplicative data collection. Universal developments in information technology, like the creation of distributed data networks and virtual data access, provide ways to address clinical research needs that did not exist before. It is time to exploit and enhance these technologies to support clinical trauma research.

The consolidation and linkage of data sets in a shared data repository would greatly expand their use and provide a robust scientific platform; pooled data sets can create the additional statistical power necessary to improve statistical significance. This clinical research repository employing common data elements will be particularly beneficial in maximizing trauma study data because it is often difficult to obtain informed consent since the injury and the need for early interventions often coincide; the patient is often unable to give consent due to the level of consciousness; and family are often unavailable in the early stages of treatment after trauma. The ability to make aggregated research data widely available to clinical investigators is critical to reform trauma research and care because, while the practice of medicine should be evidence-based, within the field of trauma there is surprisingly little evidence to support clinical practice. The formation of a national trauma research repository will ensure maximum utilization of trauma data for translation into evidence-based practice. The NTRR will be built as a scalable, customizable repository that is capable of receiving data feeds from other data systems through a conversion method. NTRR will be structured such that any study can contribute any portion of its data, besides the core common data elements, and those elements remain linked to the original source as well as available for secondary analysis in concert with any other data set. The initial module will be a set of generic data elements that is as globally representative across all trauma patients as possible yet is robust enough to support a data analysis plan. Dissemination of research outcomes will be diverse and multipronged. NTI's role is to support the study PIs development of presentations and preparation of manuscripts and to magnify those efforts through a comprehensive

communications strategy. This strategy to communicate published work includes NTI website announcements and content, blog posts, electronic communications and newsletters, white papers for external audiences, social networking, and physical distribution of reprints. The goal is to comprehensively disseminate published works to the wider trauma network.

Progress Reported:

The **National Trauma Research Repository (NTRR)** Steering Committee was formed under previous funding and includes members of stakeholder organizations and the DoD. This committee provides oversight and governance of the project. Individuals were chosen because of national leadership positions, experience with database development, and/or other subject matter expertise. An Executive Committee of the larger body established four subcommittees of injury researchers and technical experts: Architecture, Regulatory/Human Subjects Protection, Data Definitions and Policies and Procedures.

National Trauma Research Repository Steering Committee

Organization Represented	Name	Home Institution
Coalition for National Trauma Research (CNTR), Clinician Scientists and Other Stakeholders	Don Jenkins, MD—Chair	Mayo Clinic
	Eileen Bulger, MD—Vice-chair	University of Washington
	Peggy Knudson, MD	UC-San Francisco
	Jerry Jurkovich, MD	Denver
	Greg Beilman, MD	University of Minnesota
	Joe DuBose, MD	Travis AFB
	Alex Valadka, MD	Virginia Commonwealth University
	Jason Sperry, MD	University of Pittsburgh
	Ellen MacKenzie, PhD	Johns Hopkins University
	Avery Nathens, MD	Sunnybrook HSC, Toronto
	Jim Ficke, MD	Johns Hopkins University
American College of Surgeons/Committee on Trauma	Ronny Stewart, MD	UTHSC—San Antonio
	Len Weireter, MD	Eastern Virginia Med. School
Department of Defense	LTC Kyle Remick, MD	CCRP, Military Deputy
	Jose Salinas, PhD	USAISR, San Antonio
	Mary Ann Spott, PhD	Dep. Dir. Joint Trauma System
	Tammy Crowder, PhD	CCCRP, Trauma Portfolio
	Frank Lebeda, PhD	MRMC, Dir. System Biology
National Institutes of Health	Matt McAuliffe, PhD	NIH, CIT, Bethesda MD

Note: Grayed background denotes members of Executive Group of the Steering Committee

NTRR Subcommittees

Architecture	Human Research Protections/Regul.	Data Definitions	Policies & Procedures
Jose Salinas	Len Weireter	Greg Beilman	TBN
Matt McAuliff	Peggy Knudson	Alex Valadka	Joe DuBose
Avery Nathens	Eileen Bulger	Jim Ficke	Ellen MacKenzie
Ronny Stewart	Mary Ann Spott	Jerry Jurkovich	
	Laura Brosch	Mary Ann Spott	

Note: Grayed background denotes subcommittee chair.

The subcommittees were established and charged as follow:

1. Architecture—Determine functional requirements of the physical product, reviewing how other clinical research databases are built and desired level of compatibility with related products such as the FITBIR informatics system; consider how to build the back end and front end of the database, including a plan for data quality and validation, report writing, and the user help desk.
2. Regulatory/Human Protections—Develop complete understanding of factors including protections/use of military data; established regulations in other research databases; how to meet or exceed requirements for human subject research protections; recommendations for future hosting of NTRR based on regulatory or human research protection requirements. Develop guiding policies and procedures on Data Sharing, Data Submission Requests.
3. Defining Data—Identify Common Data Elements and a well-defined data dictionary, following review of assembled elements from other trauma research databases (GLUE grant, ROC, etc.)
4. Policies & Procedures—Develop standards operating procedures and management policies for launching and maintain the NTRR.

The Architecture Subcommittee met and developed user requirements for NTRR which has since been transcribed into a formal Requirements Definition (Appendix E). NTI/NTRR project staff have identified and reviewed the top 10 programming languages for front-end and back-end (database) websites and presented this information to the Architecture subcommittee. Several existing platforms have been reviewed in-depth with online demonstrations (such as Research Electronic Data Capture (REDCap), FITBIR, and Biologic Specimen and Data Repository Information Coordinating Center (BioLINCC)). This committee also developed Use Case Scenarios for the various users of the repository (Appendix F). Most recently NTI project staff developed a draft request for proposal (RFP) and statement of work (SOW) which are under review by the Architecture Subcommittee.

The Human Subject Protection/Regulatory Subcommittee has drafted several policy documents based on FITBIR policies for data sharing, data contribution, data requesting, and the use of deidentified data only. A Policy on Policies (Appendix G), which describes all regulatory references applicable to any policy, has been written and is being reviewed by the DoD for DoD-specific data management issues (by Laura Brosch). The subcommittee also developed a Data Storage and Sharing Policy (Appendix H) and a Data Access Request and Data Use Certification Policy (Appendix I).

The Data Definitions Subcommittee: The NTI/NTRR project staff have reviewed more than 30 existing research databases, registries, and repositories and over 1,000 common data elements. Trauma specific registries/repositories included in this review were the Glue Grant, FITBIR, The Prospective, Observational, Multicenter, Major Trauma Transfusion (PROMMTT) Study, The Resuscitation Outcomes Consortium (ROC), National Trauma Data Standards (NTDB), National Burn Data Standards (NBDS), and the National Emergency Medicine Information System (NEMSIS). Common data elements were ranked in order of frequency across datasets and then evaluated by the Data Definitions Subcommittee. The subcommittee recommended an initial 18 clinical CDEs and 45 study attributes or meta-study data elements.

Additional clinical CDEs and unique data elements will be drawn from the PROOVIT and Ketamine studies funded by this grant. Using the CDEs selected by the Data Definition Subcommittee, NTI project staff have created the NTRR data dictionary with 31 standardized data attributes for each element. The dictionary uses already widely accepted data definitions/parameters from existing trauma and related research registries, and data from previous and upcoming studies (under this contract).

These subcommittees began meeting in Spring 2016 and largely completed their work by end of Year 1 (Appendices D – H).

Providing a forum for dissemination of research outcomes to the trauma community: Dissemination of trauma research was diverse and multipronged in Year 1 of this agreement. NTI supported the study PIs development of presentations and preparation of manuscripts (Appendices A, C, and D) and magnified those efforts through a comprehensive communications strategy. This strategy to communicate published work includes NTI website announcements and content, blog posts, electronic communications and newsletters, white papers for external audiences, social networking, and physical distribution of reprints. In Year 1, the NTI website had an average of 1,109 users per month. NTI communicated with the trauma stakeholder community regarding research findings via 10 communiques to 4,625 subscribers. NTI also tweeted 75 trauma research-related messages to 641 followers. Additionally, 26 blog posts regarding trauma research advances were posted on the NTI website (www.nationaltraumainstitute.org). The goal is to comprehensively disseminate published works to the wider trauma network through a Knowledge Translation Plan thereby accelerating the adoption of research findings to improve civilian trauma and combat casualty care and outcomes (Appendix J).

Study/Projects Major Tasks and Accomplishments in Year 1

Study 1 KETAMINE STUDY	**Timeline in Months**	**Actual completion date**	**% of completion**
Major Task 1: Prepare and adapt Research Protocol for DoD Funded Status for Study 1			
Subtask 1: Refine research protocol	1-3	06/28/2016	100%
Refine eligibility criteria, exclusion criteria, screening protocol, enrollment protocol	1-3	06/28/2016	100%
Finalize consent form and human subjects protocol	1-3	06/28/2016	100%
Coordinate IRB protocol submission	1-3	06/28/2016	100%
Submit for Military 2nd level IRB review (ORP/HRPO)	3-6		75%
Submit amendments, adverse events and protocol deviations as needed	6-18		N/A
Milestone Achieved: Protocol for Study 1 developed	3	6/28/2016	100%
Milestone Achieved: Local IRB approval	4-5		95%

Milestone Achieved: HRPO approval	8		0%
Major Task 2: Data Analysis for Study 1			
Subtask 1: Monitor data collection and data quality	8-20		0%
Study 2 PROOVIT STUDY			
Major Task 3: Adapt PROOVIT Protocol for DoD Funded Status for Study 2			
If applicable, coordinate with sites for IRB protocol submission	1-6	01/05/2016	100%
Coordinate with sites for Military 2nd level IRB review (ORP/HRPO)	1-6	03/31/2016	100%
Submit amendments, adverse events and protocol deviations as needed	As needed	09/29/2016	100%
Coordinate with sites for annual IRB report for continuing review	Annual	09/29/2016	100%
Prepare and submit quarterly progress report to DoD	Qrtly	09/29/2016	100%
Milestone Achieved: Local IRB approval at all sites	3	03/29/2016	100%
Milestone Achieved: HRPO approval for all protocols	6	04/22/2016	100%
Major Task 4: Subcontract with all Study Sites for Study 2			
Verify sub-award documents: budget, budget justification, salary verification	1-3	3/22/2016	100%
Issue and execute sub-award document	1-3	3/22/2016	100%
Receive quarterly progress reports	Qtrly	09/29/2016	100%
Review quarterly progress reports	Qtrly	09/29/2016	100%
Milestone Achieved: Subawards issued for all sites	3	3/22/2016	100%
Major Task 5: Data Analysis for Study 2			
Subtask 1: Coordinate with sites and NTI for monitoring data collection rates and data quality	4-6		50%
Perform all analyses according to specifications, share output and finding with all investigators	Ongoing		10%
Project 1 SURGICAL AIRWAY SIMULATOR			
Major Task 6: Develop High Fidelity Airway Simulator			
Execute Subaward	1	05/12/2016	100%
Develop a model base	1-4	07/01/2016	100%
Engineer hydraulic, mechanical and pneumatic systems for head movement, airway lubrication, respiration and circulation	1-4	07/01/2016	100%

Develop and integrate a programmable logic controller	1-4	7/06/2016	100%
Integrate subsystems into the infrastructure built upon the base	5-9		
Develop a layered, high-fidelity anatomical model for face, neck and upper thorax	5-9		
Separate the components of high-fidelity anatomical model for molding	5-9		
Create molds of the anatomical components including bones, selected individual muscles, fascia, larynx, trachea, thyroid gland, major arteries and veins	10-12		
Create serial iterations of the models and molds to complete engineering	10-12		
Research materials for high anatomical and surgical fidelity laryngo-tracheal complex	10-12		
Project 2: NATIONAL TRAUMA RESEARCH REPOSITORY			
Major Task 8: Determine Data Dictionary and Vendor Requirements			
Coordinate with Steering Committee to determine Common Data Element Workgroup	1-3	03/29/2016	100%
Common Data Element Determinations	1-6		95%
Develop Data Dictionary	6-9		95%
Milestone Achieved: Data dictionary			
Major Task 9: Vendor solicitation and selection			
Determine repository requirements	1-6	08/11/16	100%
Vendor solicitation and selection process	6-9		20%
Milestone Achieved: Repository requirements document		08/11/16	100%
Milestone Achieved: Vendor Selected			
Major Task 10: Repository build and testing			
Repository build (back and front end)	9-12		0%
Major Task 11: Website development and policy			
Develop management policies	3-9		95%
Develop website and interfaces	6-15		0%
Milestone Achieved: Policies available on functional website			

Training and Professional Development

Nothing to report.

Dissemination of Results to Communities of Interest

Although we do not have study findings or completed projects, there were three opportunities for disseminating information to communities of interest in Year 1.

Study 1: Determining the Efficacy and Safety of Ketamine as a Battlefield Analgesic

The Study 1 team presented a poster depicting the protocol for the "Ketamine for Acute Burn Pain" project at a local Behavioral Pharmacology Research Unit conference (Appendix A).

Project 2: National Trauma Research Repository

The project PI (Dr. Donald Jenkins) and the NTI study team were invited to submit a manuscript detailing the work underway for this contract for the 2016 Shock Military Supplement. The team prepared a manuscript detailing the development of the National Trauma Research Repository and submitted it in May 2016. It was accepted and published in the Military in August 2016 (Appendix C).

Additionally, the project PI (Dr. Donald Jenkins) and the NTI study team were invited to present at the 2016 Military Health System Research Symposium during the Surgical Critical Care and Burn Session moderated by Dr. Jose Salinas. The presentation detailed work completed previous DoD funded projects with the National Trauma Institute and introduced the National Trauma Research Repository under for this grant (Appendix D).

Plans for the Next Quarterly Reporting Period

Study 1 - Determining the Efficacy and Safety of Ketamine as a Battlefield Analgesic

The study team will receive local IRB approval, submit the protocol to HRPO, receive HRPO approval and initiate participant enrollment. Data collection processes, data quality, and participant accrual rates will be monitored. The team is also preparing a manuscript depicting the protocol to submit for publication (which will include 3 pilot cases).

Study 2 – PROOVIT Study

A request for a Statement of Work modification will be submitted to add East Carolina University as an additional PROOVIT clinical site for a twelve-month period of performance. Budget, budget justification, and salary verification are currently under review. Continue to enroll subjects, monitor data quality, accrual rates at all sites. The PI and NTI/NTRR staff will look at recruitment barriers at Wisconsin and determine whether they should continue as a site.

Project 1 – Airway Management Simulator

Operative Experience, Inc. (OEI) will submit their second quarterly report on 11/01/2016 providing updates on the activities scheduled for months 3-6 in the Scope of Work. Based on their later initiation date, the original statement of work will be adjusted. National Trauma Institute staff will meet regularly with the OEI team to monitor simulator development. OEI will

continue the development of high fidelity airway management simulator technology as described in the Scope of Work.

Project 2 – National Trauma Research Repository

The NTRR Executive Committee will continue discussions with National Institutes of Health regarding developing the NTRR in collaboration with the Center for Information Technology, the National Institute for Neurological Diseases and Stroke and alignment with the Federal Interagency for Trauma Brain Injury Research (FITBIR) Informatics System. A vendor (NIH or other) will be selected to build the repository application per the requirements document and use case description (Appendices E and F). A subcontract will be issued and the vendor will begin to build the application in close collaboration with NTI staff. Data elements (common data elements and unique data elements) will continue to be refined for the repository. The initial common data elements selected are linked to the vendor/product selected for the repository in that the vendor selected will already have fully developed/defined CDEs that may be adopted for the NTRR. Also, the CDEs selected for the initial NTRR will be influenced by ongoing strategic planning by the NTRR Executive Committee short and long term analysis plans. Unique data elements from the ongoing studies under this project (Ketamine and PROOVIT) will be identified and defined. The Policies and Procedures subcommittee will develop additional standards, policies and operating procedures in Year 2. Data sharing, data submission and data sharing policies will continue to be refined.

NTI staff will continue to implement the Knowledge Translation Plan in the next quarter (Appendix J). NTI staff working on this project will attend the “Communication Tools for Moving Research to Practice” conference that will be held October 24, 26, 28, 2016. This annual on-line conference is hosted by the Center on Knowledge Translation for Disability and Rehabilitation Research. It is designed for researchers to learn about current and innovative communications tools, including social media, in order to increase the use of evidence-based research findings through knowledge translation activities. Lessons learned from this conference will be used to update and improve the knowledge translation plan and support translation of study findings and products to military and civilian trauma audiences.

IMPACT

As we have just completed Year 1 of a three-year period of performance, there are no developments in the principal discipline, other disciplines, technology transfer or to society beyond science and technology to report at this time.

CHANGES/PROBLEMS:

There are no changes in the approach for this work. The IRB approval for the Ketamine study is taking slightly longer than anticipated therefore the enrollment targets for this study will be adjusted according to the IRB and HRPO approval dates. This will not affect the overall Agreement period of performance as Dr. Fauerbach is confident he can complete his study in one year. The contracting process with OEI took longer than expected therefore the deliverable timeline will be adjusted. The initial deliverable timeline was based upon the timeframe for this Agreement and is now adjusted to meet the period of performance of the Contract with OEI. This will not affect the overall period of performance for this Agreement. There are no changes that impact expenditures or in the care of human subjects.

The NTRR development funded through this Agreement is intended to be the initial development and further development and sustainment funding is recognized as necessary. The DoD and NTI met at MHSRS to discuss the progress of the NTRR project and the need for further development and sustainment funding.

PRODUCTS:

1. Song, A., Gerold, K., McCann, U.D., Caffrey, J., Latif, A., Milner, S.M., Fauerbach, J.A. Safety and Efficacy of Ketamine as a Battlefield Analgesic for Acute Burn Pain. Poster presentation at the Asthma and Allergy Center of Johns Hopkins Bayview Medical Center in Baltimore, MD, July 27, 2016. (Status: Presentation completed; Acknowledgement of federal support: No)

2. Smith SL, Price MA, Fabian TC, Jurkovich GJ, Pruitt BA, Jr., Stewart RM, et al. The National Trauma Research Repository: Ushering in a New ERA of trauma research (Commentary). Shock. 2016;46(3 Suppl 1):37-41. (Status: Published; Acknowledgement of federal support: Yes)

3. Jenkins, DH. Impact of Department of Defense Research to the National Trauma Institute. Presented at the Military Health System Research Symposium, Orlando FL, August 17, 2016. (Status: Presentation completed; Acknowledgement of federal support: Yes)

PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

NTRR Participants

Name	Project Role	Nearest person month worked	% Effort	Contribution to the project
Donald Jenkins	Principal Investigator	0.6	5%	Oversight of entire project
Roy Estrada	Program Manager	9.84	82%	Regulatory oversight and coordination of regulatory reviews and reporting for the 13 research subawards. Data element review.
Monica Phillips	Research Operations Director	8.4	70%	Subaward document preparation, negotiation, and execution for 12 subawards. Assist in data element review. Attends all committee meetings.
Ana Guerrero	Admin Support	6.0	50%	Coordinating Steering Committee meetings, drafting minutes, planning face to face steering committee meeting.
Pam Bixby	Communications	3.0	25%	Responsible for the communication and dissemination tasks of the projects and for broader trauma research

				dissemination according to the Knowledge Translation Plan
Sharon Smith	Project Administrator	5.64	47%	Managing Steering Committee meetings, agenda, process. Establishment of working groups.
Michelle Price	Co-Investigator	6.5 (started mid-Feb)	100%	Conducting research on existing registries, platforms, and common data elements. Coordinating subcommittee work and meetings. Communicating with stakeholders and potential collaborators at DoD, NIH, academic trauma centers and trauma professional organizations.

There are no changes in the active other support for the PI or key personnel.

Other Collaborating Organizations

Organization	Location	Contribution to Project
Baylor College of Medicine/Ben Taub Hospital	1504 Taub Loop, Houston, TX 77030	PROOVIT Clinical Site (PI: Dr. Ramyar Gilani)
Emory University	201 Dowman Drive, Atlanta, GA 30322	PROOVIT Clinical Site (PI: Dr. Ravi Rajani)
Loma Linda Medical Center	11234 Anderson Street, Loma Linda, CA 92354	PROOVIT Clinical Site (PI: Dr. Richard Catalano)
University of Southern California	1983 Marengo Street, Los Angeles, CA 90033	PROOVIT Clinical Site (PI: Dr. Kenji Inaba)
Scripps Health	4077 Fifth Avenue, San Diego, CA 92103	PROOVIT Clinical Site (PI: Dr. Steven Shackford)
University of California, Davis	2315 Stockton Boulevard, Sacramento, CA 95817	PROOVIT Clinical Site (PI: Dr. Joseph Galante)
University of Maryland/Shock Trauma	22 S. Greene Street, Baltimore, MD 21201	PROOVIT Clinical Site (PI: Dr. Thomas Scalea)
University of Tennessee – Memphis	920 Court Street, Memphis, TN 38163	PROOVIT Clinical Site (PI: Dr. Timothy Fabian)
University of Texas Health Science Center at Houston	6410 Fannin Street, Houston, TX 77030	PROOVIT Clinical Site (PI: Dr. John Holcomb)
University of Wisconsin School of Medicine and Public Health	750 Highland Avenue, Madison, WI 53276	PROOVIT Clinical Site (PI: Dr. Suresh Agarwal)
Wright State University	1 Wyoming Street, Dayton, OH 45409	PROOVIT Clinical Site (PI: Dr. John Bini)
University of Texas Health Science Center at San Antonio	7703 Floyd Curl Drive, San Antonio, TX 79230	PROOVIT Statistical Analysis (PI: Dr. Joel Michalek)
Johns Hopkins University	600 North Wolfe Street, Blalock 1415, Baltimore, MD 21287	Ketamine Clinical Site (PI: Dr. John Fauerbach)
Operative Experience, Inc.	500 Principio Parkway West, Suite 300, North East, MD 21901	Airway Management Simulator Development (PI: Dr. Robert Buckman)

SPECIAL REPORTING REQUIREMENTS

The Quad chart for this project follows.

APPENDICES:

A. Safety and Efficacy of Ketamine as a Battlefield Analgesic for Acute Burn Pain. Poster presentation

B. High Fidelity Simulator for Training Airway Management of Combat-Relevant Wounds of the Face and Neck

C. The National Trauma Research Repository: Ushering in a New ERA of trauma research

D. Impact of Department of Defense Funded Research at the National Trauma Institute

E. National Trauma Research Repository (NTRR) Requirements Definition

F. National Trauma Research Repository (NTRR) Use Cases

G. National Trauma Research Repository (NTRR) Policy on Policies

H. National Trauma Research Repository (NTRR) Data Storage and Sharing Policy

I. National Trauma Research Repository (NTRR) Data Access Request, Data Use Certification Policy and Data Submission Request

J. National Trauma Institute's Knowledge Translation Plan → Moving Knowledge into Action

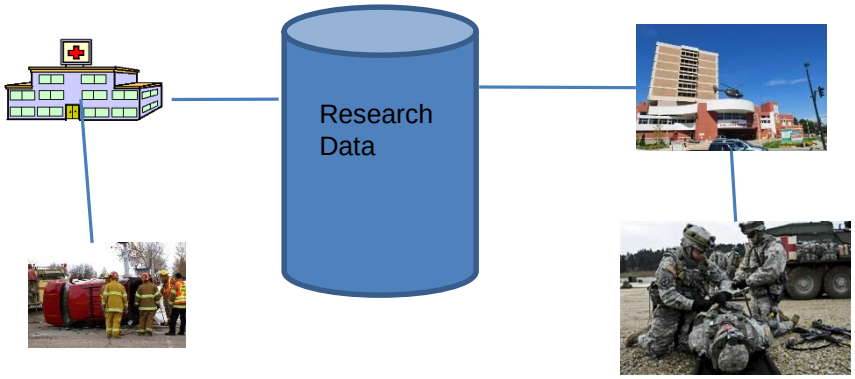
A National Coordinating Center for Trauma Research

PI: Donald Jenkins, MD **Org:** National Trauma Institute

Study/Product Aim(s)

Hypothesis: The civilian trauma research community can be used as a surrogate for military combat casualty care research, maximizing the return from dollars invested by replacing the expensive and repetitive assembly and disassembly of short-lived clinical investigator networks with a stable and enduring operational infrastructure for clinical trauma research.

- Technical Objective 1: To manage specific research projects addressing military research gaps in airway management, pain management and vascular injury.
- Study 1: Determining the Efficacy and Safety of Ketamine as a Battlefield Analgesic;
- Study 2: The PROspective Observational Vascular Injury Trial (PROOVIT);
- Project 1: High Anatomic Fidelity Surgical Airway Training system;
- Technical Objective/Project 2: Develop tools to allow or the collection and dissemination of results and data from studies.



Timeline and Cost (direct + indirect)

Activities	FY16	FY17	FY18
Ketamine Study			
Airway Simulator Development			
PROOVIT			
NTRR Development			
Total Budget ($M)	$2.1M	$1.4M	$1.1M

Goals and Milestones

CY16 Goal –
- ❑HRPO approval for studies (Study 1 pending IRB/HRPO approval)
- ☑Subcontracting complete
- ❑Studies commence (Study 1 pending IRB/HRPO approval)
- ☑Common Data Elements and NTRDB functional requirements

CY17 Goals
- ❑Ketamine study concludes
- ❑Airway simulator developed
- ❑PROOVIT study continues
- ❑NTRDB developer solicited and chosen
- ❑CY 18 Goals
- ❑NTRDB development and testing

Comments/Challenges/Issues/Concerns: none at this time

CDR Alexis Mosquera (301-619-7906/alexis.mosquera.mil@mail.mil)

Safety and Efficacy of Ketamine as a Battlefield Analgesic for Acute Burn Pain

Alex Song, Kevin Gerold, Una D. McCann, Julie Caffrey, Asad Latif, Stephen M. Milner, James A. Fauerbach

[1] Departments of Plastic and Reconstructive Surgery, Anesthesia and Critical Care Medicine, Psychiatry and Behavioral Science, Johns Hopkins University School of Medicine, Baltimore, MD, USA

Introduction

- The acutely painful, twice-daily wound care necessitates finding effective analgesic medication regimens with fewer side effects than morphine
- Morphine analgesic is the usual care (UC-O) of burn patients
- UC-O requires repeated dosages which can lead to opiate induced hyperalgesia and morphine tolerance
- Ketamine is an analgesic that blocks nociceptive signals to the brain via a pathway that differs from opiate analgesics and thus may have opiate sparing effects
- Ketamine may also reduce symptoms of PTSD and depression

Background

- Wound care occurs 1-2 times per day
- Repeated wound care may cause increased sensitivity of nociceptive receptors and risk for developing chronic pain
- Few studies have been conducted testing the efficacy of ketamine augmentation of opiates for acute burn wound care or ketamine's hypothesized opiate sparing effect

Objectives

The study is conducted to address the following objectives:

Primary

- Whether ketamine augmentation to usual opiate care (K+O) reduces burn pain during wound care
- Whether ketamine is associated with opiate sparing effect during wound care

Secondary

- Whether the prevalence and severity of Acute Stress Disorder (ASD),PTSD, and depression are reduced by the K+O condition to UC-O
- Whether symptoms of pain-related anxiety and pain-related catastrophizing are reduced by the K+O condition compared to UC-O
- How the K+O condition can improve sleep quality and effect duration
- How emotion regulation and trauma resilience can moderate pain-related anxiety and catastrophizing

Study Design

- Double-blind, parallel-group, randomized controlled trial
- Sample is drawn from population of consecutive admissions to Johns Hopkins Burn Center
  - 300 Screened, 150 enrolled
- Groups are stratified based on Total Body Surface Area (TBSA)
  - 60% of sample will be small burns (≥2% and ≤ 20% TBSA)
  - 40% of the sample will be "moderate" burns (>20% and ≤40% TBSA)

Participant Inclusion Criteria:

- Acute burn injury with TBSA ≥2% & ≤40%.
- Adults 18-65 years of age admitted to the JHBC with acute burns
- Estimated length of stay ≥7 days
- Pain in Emergency Room during initial wound evaluation (NAS ≥6)

Participant Exclusion Criteria:

- Requiring endotracheal intubation and sedation
- Diminished Level of Consciousness / Cognitive Function (MMSE ≤20)
- Diminished Capacity – Incapable of providing informed consent
- PMH: Insensate (e.g., SCI)
- Safety: Contra-indication (e.g., potential drug interactions, medical comorbidities)

Materials and Methods

The following will be measured (see Figure 2 for measures and timing):

Comparing effectiveness of K+O to UC-O in reducing severity of acute pain

- *Self-reported pain* using a Numerical Analog Scale (NAS) – measurement is standardized by applying pressure at wound, proximal and distal regions, before, during and after wound care
- *Sympathetic arousal* using the Itamar Watch-PAT 200
- *Time to maximal pain relief* – time taken to achieve lowest pain rating on NAS from the time that each wound care procedure begins
- *Recollection of pain* using NAS
- *Satisfaction with wound care* using a visual analog scale

Opiate sparing effect

- Frequency of requests for additional analgesic medications

Post-treatment effect

- During a follow-up assessment, 1 month after the study protocol:
  - *ASD/PTSD* using the Diagnostic and Statistical Manual of Mental Disorders IV – Text Revision (DSM IV-TR)
  - *Depression* using the Beck Depression Inventory (BDI-II)
  - *Sleep and sympathetic reactivity* using the Itamar Watch-PAT 200
  - *Trauma Resilience* using the Trauma Resilience Scale
  - *Optimism* using the Life Orientation Test
  - *Emotion Regulation* using the Emotion Regulation Scale State

Study Diagram and Participant Flow

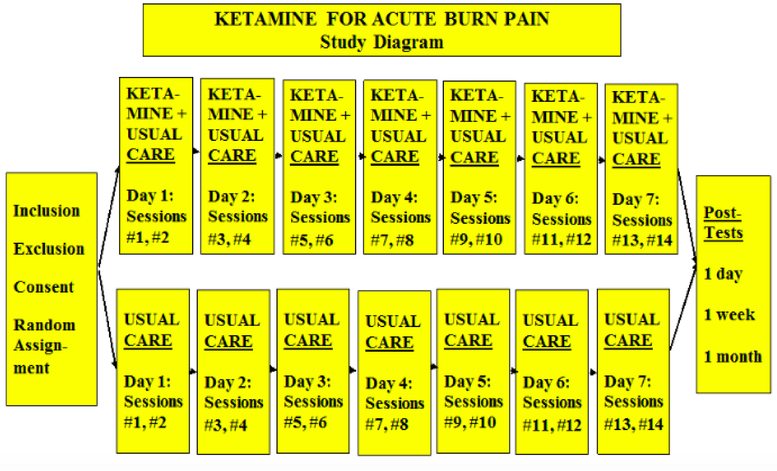


Figure 1

- 1.25 months
- 1 day pretest baseline
- 7 days of twice daily interventions
- Follow-up at 1 day, 1 week and 1 month after the 7th day (14th session)

Assessment: Measures and Timing

Ketamine For Acute Burn Pain: Assessment Diagram

PRIOR TO RANDOM-IZATION: (Examples)	BASELINE: PREBURN MONTH (Retrospective)	Days: 1 – 7 Sessions #1 - #14:	Days: 3, 5, 7 Sessions: #6, #10, #14 Additional measures as follows:	POST-TESTS After final procedure:
Inclusion TBSA: ≥2% & ≤40% **Exclusion** Pain <6/10 in ER **Stratification** TBSA: ≥2%-≤20% >20%-≤40%.	**Month Before Burn** (Retrospective) Pain – Average NAS Type, Location Pain Medications Pain Anxiety Symptom Scale (PASS) Pain Coping Questionnaire. Pain Catastrophizing PTSD (SCL-C) Depression (BDI-II) Behavior Inhibition / Behavior Activation Scales (BIS/BAS) Post-Trauma Resilience Scale (PTRS) Emotion Regulation Scale (ERS)	**Before Session (~1 hour)** Burn Pain NAS Every 10 minutes during procedure at: Wound Proximal to wound Distal to wound Pain Medications Acute Stress Disorder Depression **During Session** Burn Pain: NAS every 10 minutes during procedure: - Locations as above Additional Analgesic Medications **After Session** Burn Pain: NAS 1 hour & 6 hours Pain Management Satisfaction	**Prior to Session** Pain Anxiety (PASS) Pain Coping Pain Catastrophizing All other pre-session measures as shown in prior box for Sessions 1-14. **During Session** All intra-session measures as shown in prior box for Sessions 1-14. **After Session** All post-session measures as shown in prior box for Sessions 1-14.	**Day 1** Burn Pain (Mean 24-hr NAS) at Locations: Wound Proximal to wound Distal to wound Pain Medications Pain Management Satisfaction **Week 1:** All Day 1 post-test follow-up measures as above. **1 Month:** All Day 1 & 6 post-test follow-up measures, plus: PTSD (SCL-C) Depression (BDI-II) Resilience (PTRS) Emotion Regulation (ERS)

Figure 2

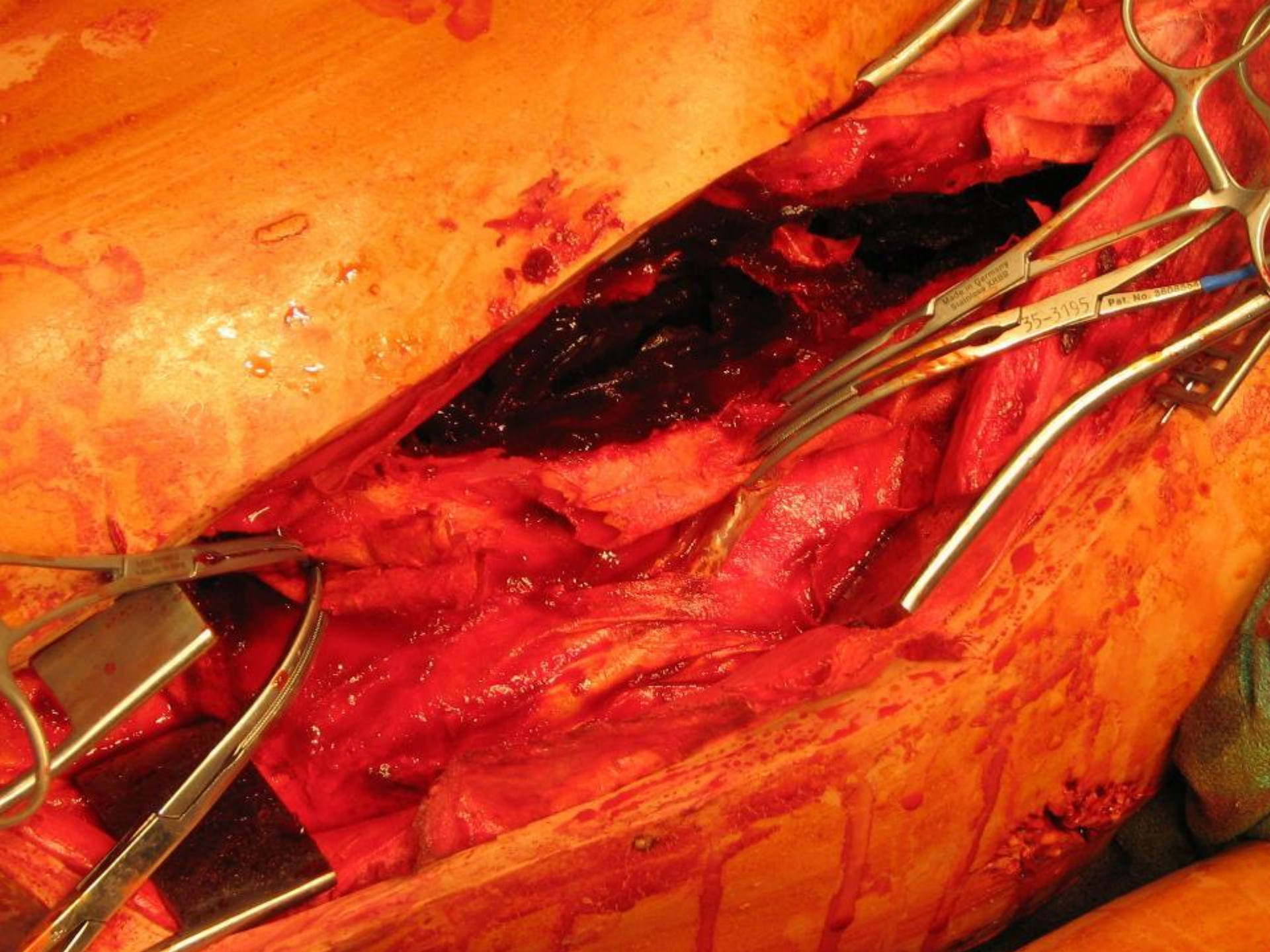
High fidelity simulator for training airway management of combat-relevant wounds of the face and neck

Train medics and surgeons

:

Biofidelic Emulation™ vs Simulation

electromechanical mechanisms within realistic surgical anatomy and tissues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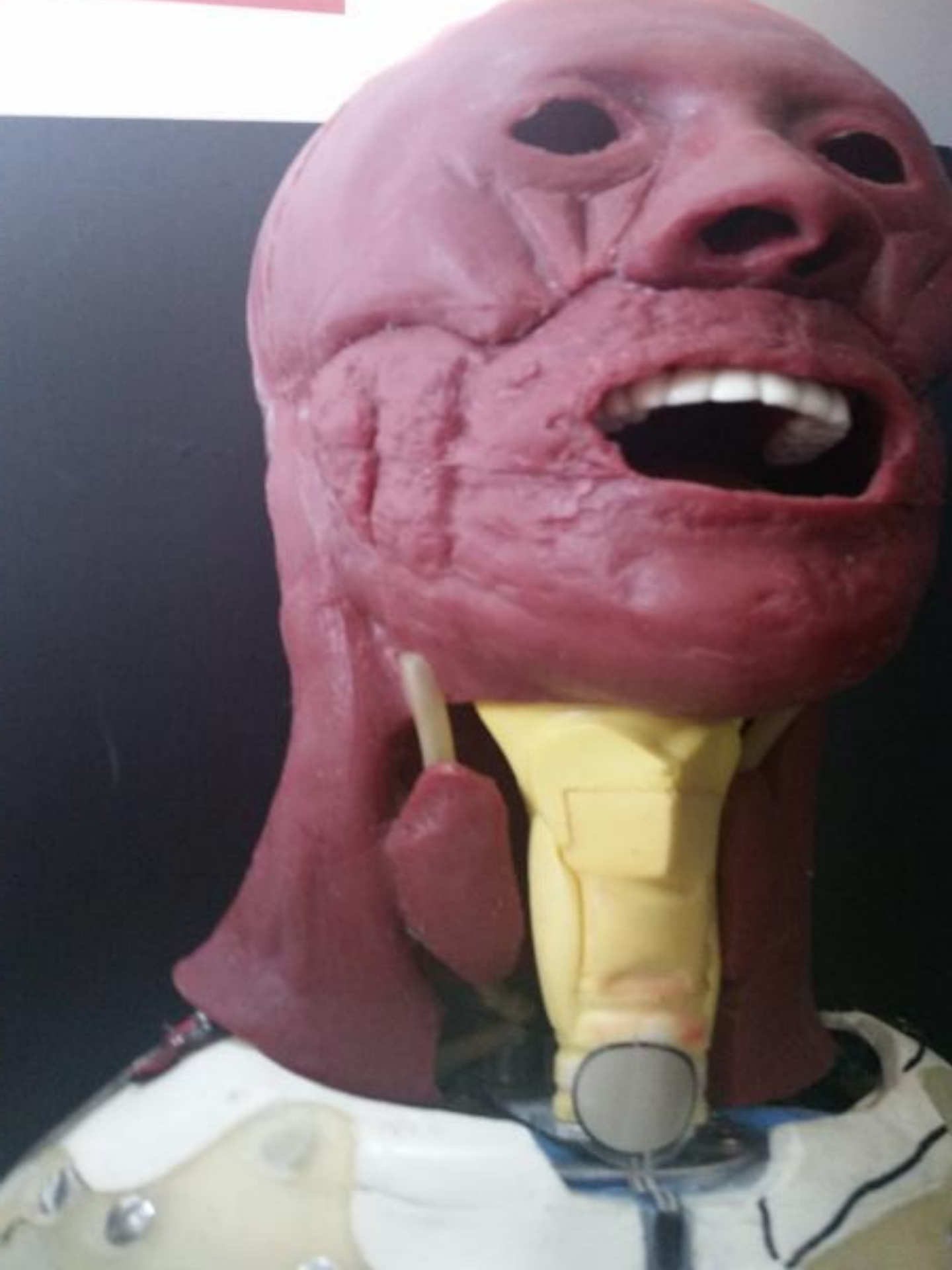
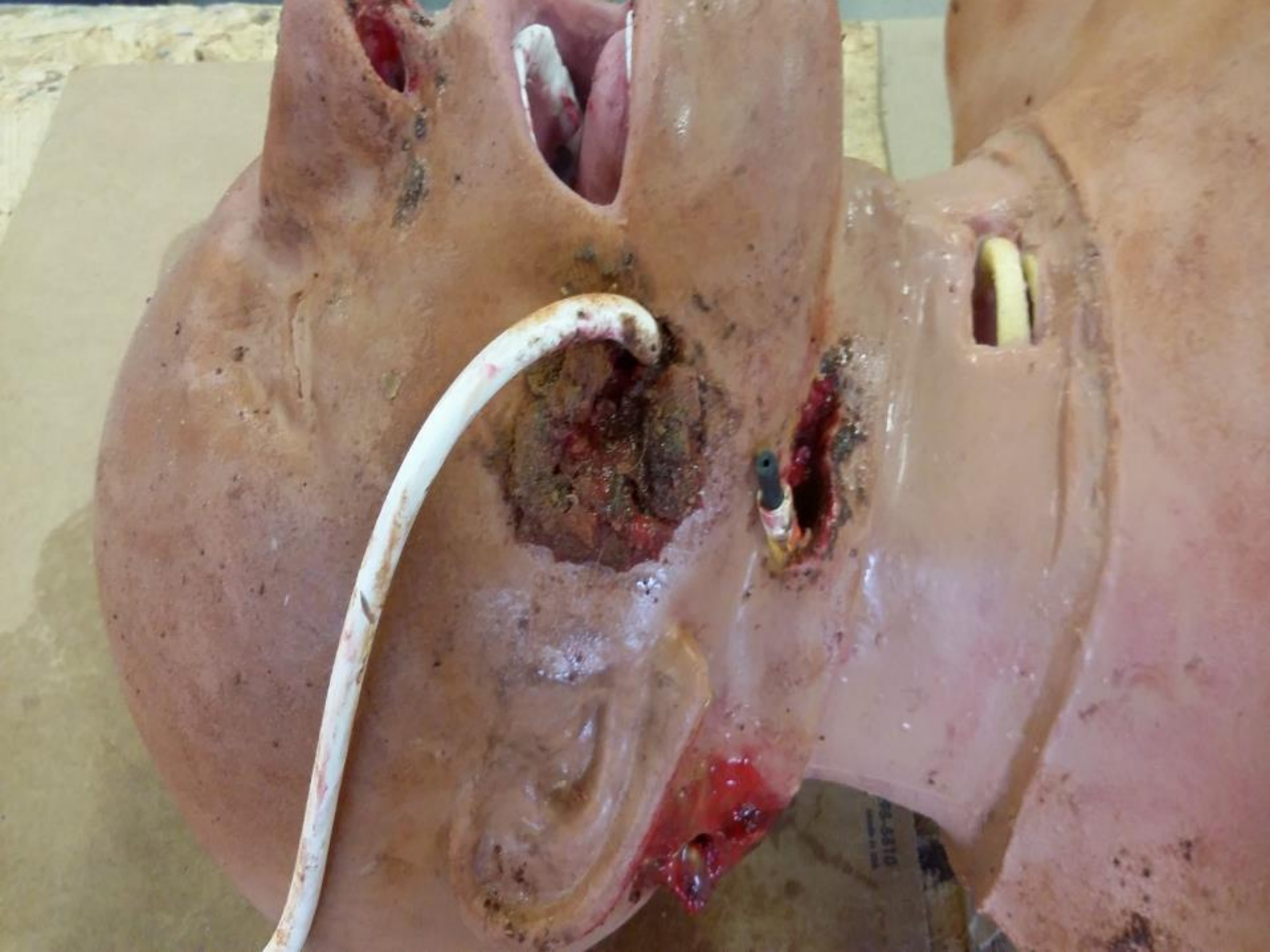
We are engineering electromechanical and hydraulic systems
to fit within a unique, high anatomical fidelity construct of the head, face, neck and upper chest.

Anatomic and tissue modelling





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THE NATIONAL TRAUMA RESEARCH REPOSITORY: USHERING IN A NEW ERA OF TRAUMA RESEARCH (COMMENTARY)

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ABSTRACT—Despite being the leading cause of death in the United States for individuals 46 years and younger and the primary cause of death among military service members, trauma care research has been underfunded for the last 50 years. Sustained federal funding for a coordinated national trauma clinical research program is required to advance the science of caring for the injured. The Department of Defense is committed to funding studies with military relevance; therefore, it cannot fund pediatric or geriatric trauma clinical trials. Currently, trauma clinical trials are often performed within a single site or a small group of trauma hospitals, and research data are not available for secondary analysis or sharing across studies. Data-sharing platforms encourage transfer of research data and knowledge between civilian and military researchers, reduce redundancy, and maximize limited research funding. In collaboration with the Department of Defense, trauma researchers formed the Coalition for National Trauma Research (CNTR) in 2014 to advance trauma research in a coordinated effort. CNTR's member organizations are the American Association for the Surgery of Trauma (AAST), the American College of Surgeons Committee on Trauma (ACS COT), the Eastern Association for the Surgery of Trauma (EAST), the Western Trauma Association (WTA), and the National Trauma Institute (NTI). CNTR advocates for sustained federal funding for a multidisciplinary national trauma research program to be conducted through a large clinical trials network and a national trauma research repository. The initial advocacy and research activities underway to accomplish these goals are presented.

KEYWORDS—Advocacy, clinical trials network, data-sharing, injury, research funding, trauma

Trauma is the leading cause of death among individuals 46 years and younger, and the single largest cause for years of life lost in the United States (1). In a review of mortality data from 2000 to 2010, Rhee et al. (1) found a 22.8% increase in trauma deaths in contrast with a decrease in deaths from cancer and heart disease. In the United States, 199,756 persons suffered fatal injury in 2014 and 30,888,063 were treated in emergency departments for non-fatal injuries in 2013 (2). Medical treatment and work loss costs for civilian fatal and non-fatal injuries in the United States totaled more than $586 billion in 2010 (2). In Operation Enduring Freedom (OEF), Operation Iraqi Freedom (OIF), Operation New Dawn (OND), Operation Inherent Resolve (OIR), and Operation Freedom's Sentinel (OFS), there have been 52,407 injured U.S. military and Department of Defense (DoD) civilians and 6,881 deaths from trauma (3). These statistics point to the dramatic burden of injuries on the health of this country in both civilian and military sectors.

It continues to surprise many that trauma, as a disease category, receives so little research funding support from the Federal government. This problem has been reviewed and restated many times over the last 50 years, and 2016 marks the 50-year anniversary of the publication that first cited the problem: ''Research in trauma has suffered from the lack of recognition of trauma as a major public health problem. The most significant obstacle at present [to trauma research efforts] is the lack of long-term funding. Unpredictability of financial support hinders recruitment of competent scientists and technicians, retention of key personnel, and procurement of necessary equipment'' (4). While this may be the first significant national publication about the lack of trauma research funding, the Institute of Medicine Committee on Injury Prevention and Control stated in 1999 that ''the nation's current investment in injury research is not commensurate with the magnitude of the problem'' and that ''without a national commitment, the field of injury science will stagnate and the unnecessary toll of injury will persist'' (5). In a 2015 report, the Agency for Healthcare Research and Quality stated that the highest condition-related expenditure total among adults ages 18 to 64, and third highest for all ages, was for treatment of trauma-related disorders (6). Without dedicated research funding, this major healthcare problem continues to worsen.

Support for sustained, long-term investment is limited, and there is diminished funding from both public and private sponsors at a time when scientific opportunity has never been greater (7). National Institutes of Health (NIH) funding of clinical trauma research is disproportionate to the burden of the disease, and by that metric, ranks last among 27 disease categories (8). In comparison with the HIV/AIDS NIH funding that exceeds the economic burden of that disease by 17%, NIH funding of injury research is 12% less than the economic burden of injuries (8).

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The authors report no conflicts of interest.

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One way of addressing these challenges lies in sharing clinical research data, as ''an opportunity to expand the investment of the clinical trial beyond its original goals at minimal costs'' (9). As the trauma research community seeks ways to extend available funds, the creation of a national repository for trauma clinical research data that makes data available for enduring use is a potentially viable and cost-effective solution. While it would not result in any additional funding, it would effectively allow for much more data analysis and knowledge translation, which can result in improved patient care.

Single-instance use of research data and the inability to access the research data of others following study closure and publication limit the effectiveness of available trauma research funding. Advances due to clinical trauma research have been accomplished largely through separate, organizationally distinct, and disconnected efforts. Individual large and successfully accomplished projects have been usually dispersed and uncoordinated by their very design and funding. This situation leads to research delays, duplications, inefficiencies, and increased costs—all part of a knowledge translation process that averages an excruciating 17 years (10).

While clinical researchers in different locations may have similar lines of investigation, the computer systems in use to store and retrieve data locally ''do not, and for the most part cannot, transmit, receive, combine, analyze and use shared data as information'' (8). In fact, it is built into the research design and data privacy tenets, directed by an Institutional Review Board, that this type of sharing cannot occur in these types of studies and research databases. Clinical research data are fragmented, sometimes within one facility, and can rarely be repurposed to answer additional research questions. Sharing data maximizes the value, promotes secondary analyses, and minimizes duplicative data collection (8, 9). Universal developments in information technology, like the creation of distributed data networks and virtual data access, provide ways to address clinical research needs that did not exist before (9). It is time to exploit and enhance these technologies to support clinical trauma research, speed up knowledge translation, and enhance the development of evidence-based trauma care practices.

BENEFITS OF CLINICAL DATA-SHARING

The Institute of Medicine reports that ''a cultural change has occurred in which the conversation around data sharing has moved from whether it should happen to how it can be carried out'' (11). Data-sharing platforms or repositories already exist for the Federal Interagency Trauma Brain Injury Research (FITBIR), the National Database for Autism Research (NDAR), the National Heart, Lung and Blood Institute (NHLBI), the Alzheimer's Disease Neuroimaging Initiative (ADNI), and other disease areas. FITBIR was developed as a joint DoD-NIH effort to share data across the entire traumatic brain injury (TBI) research field and to facilitate collaboration between laboratories, as well as interconnectivity with other information platforms. Advantages of data-sharing are numerous:

- Data-sharing reinforces open scientific inquiry and encourages diversity of analysis and opinion; enables exploration of novel topics not envisioned by the initial investigators; and facilitates the education and engagement of new researchers.
- Data-sharing avoids duplication of multiple, separate databases and results in conservation of research funds, ultimately leading to availability of funds for other studies and more investigators.
- Transfer of research and knowledge between military and civilian researchers and care providers is supported and increased in a concrete and measurable way. Research gaps are more easily identified and addressed.
- Many trauma studies require use of an expensive and lengthy process to obtain Exception from Informed Consent (i.e., community consent in place of individual consent for inclusion in a research project). This is necessary because victims of traumatic injury are frequently unconscious or otherwise unable to provide consent. Further, consent from a legally authorized representative usually can only be obtained later in the care trajectory, and life-saving intervention is necessary before the trauma victim is even identified. The ability to use data resulting from these studies may aid in the reduced need for unnecessary repetition of this process, effectively stretching limited trauma research funding.

NATIONAL TRAUMA INSTITUTE (NTI)

The National Trauma Institute (NTI), a non-profit organization chartered in 2006, has as its central purpose to advocate for trauma research funding. The members of NTI's Board of Directors are from across the United States; represent trauma and acute care surgery, emergency medicine (American College of Emergency Physicians (ACEP)), burns (American Burn Association (ABA)), neurosurgery (American Association of Neurological Surgeons (AANS)), orthopaedic surgery (Orthopaedic Trauma Association (OTA)); and include non-voting representatives from Army, Navy and Air Force medical departments. NTI has generated and/or managed nearly $55 million in trauma research funds (almost all of it in federal funds) over the past 10 years. NTI's purpose is to raise funds for trauma research, yet uniquely it does no research itself; instead, it directs those funds to the trauma clinical investigator community. Since 2008, NTI has received federal contracts to fund studies of more than 60 investigators at institutions in 35 cities and 22 states. In total, these studies have generated 16 publications (12–27), two manuscripts under review, and 23 presentations at national, regional, state, or local trauma meetings, adding substantially to the knowledge in injury care science.

In 2012, NTI leadership met with personnel within the DoD, including the Medical Research and Materiel Command (MRMC) and the Combat Casualty Care Research Program. A discussion of the challenges to adequately fund trauma research included the issue of how to make extended use of the data that result from available funding. The DoD had already funded the creation of the FITBIR platform and asked if the same could be done for the broader trauma research community. Once established, all federal trauma funding solicitations will include the requirement that funded investigators

must contribute data from studies funded by the DoD to the repository. This would create a new standard for federally-funded trauma research. Conceptually, this is precisely how the DoD Trauma Registry was developed. While not a primarily research-oriented data registry, research by ''outsiders'' can and has been carried out using the data collected for other purposes.

Following this meeting, NTI considered the concept fully. Leaders were well aware of the difficulties and risks of, first, accepting the highly technical and demanding challenge, and second, achieving success and utilization by the national trauma research community. After examination, NTI determined that a national trauma clinical research repository could be achieved if developed carefully and with the leadership and involvement of key trauma organizations and professionals and began advocating for the funding of this project within the DoD budget. In 2013, NTI developed a white paper and delivered a request for $5 million to United States House and Senate offices during the annual congressional appropriations process. The request stated that, if approved, the funds should be added to the DoD's Research, Development, Testing and Evaluation (RDT&E) program. Because of the impact on injured Americans as well as on U.S. service members wounded in combat, Congress did provide $5 million in the FY2014 Defense Health Program Research and Development budget to establish the National Trauma Research Repository (NTRR) for the purposes outlined above. Following the proposal submission and peer-review process within the DoD, NTI was the selected contractor for the NTRR.

Data stored in a fully developed and robust NTRR will cover the entire patient care trajectory: from injury prevention, to point of injury, en route care, hospital care, and finally rehabilitation/outcomes. This will be the central repository for the clinical data resulting from both military and civilian federally funded trauma research and will be a free, web-based application with a user-friendly interface for trauma researchers to contribute and access data.

CHALLENGES TO SUCCESS

Sharing data is a complex task. Beyond the challenge of encouraging full participation from investigators, including those funded by federal, state or private means, there are other challenges that include understanding the interests and privacy of study participants who volunteered their data as well as the interests of study investigators. Study investigators invest significant personal energies into the design, conduct, and analysis of studies, and tend to guard research data to retain ownership and property rights, avoid competition, reduce duplication, protect confidentiality and privacy, or avoid misuse by unqualified persons (28). Policies and procedures to protect patient and investigator rights while making data available to secondary researchers require specific and meticulous formulation (29). These are significant challenges that could undermine NTRR's success and must be addressed by project planners. Much of the work necessary to avoid these pitfalls has been accomplished or is underway, most recently by FITBIR and NADR.

PLANS FOR NTRR

The initial step was to establish a Steering Committee that includes members of stakeholder organizations and the DoD, among others, who will provide oversight and governance of the project. Individuals were chosen because of national leadership positions, experience with database development, and/or other subject matter expertise. An Executive Committee of the larger body established four subcommittees of injury researchers and technical experts: Architecture, Regulatory/Human Subjects Protection, Data Definitions and Policies and Procedures. The Architecture Subcommittee will determine functional requirements of the physical product, review structures of clinical research repositories, determine the desired level of compatibility with other repositories, application requirements including data quality and validation, report writing, and user support. The Regulatory/Human Protection Subcommittee will develop policies on human subjects protections and make recommendations for hosting of NTRR. The Data Definitions subcommittee will identify Common Data Elements to be included following review of assembled elements from trauma research repositories and other widely used common data elements. The Policies and Procedures subcommittee will develop standards, policies, and procedures such as data sharing, data submission requests, data access requests, and standard operating procedures. These subcommittees began their work in Spring 2016.

COALITION FOR NATIONAL TRAUMA RESEARCH

In 2014, the American Association for the Surgery of Trauma (AAST) and NTI began discussing the need for a unified, stronger voice to advocate for further funding of trauma research. This discussion, initially held at the headquarters of the American College of Surgeons Committee on Trauma (ACS COT), escalated rapidly, and several months later the Coalition for National Trauma Research (CNTR) was formed to include not only AAST and NTI, but also the ACS COT, the Eastern Association for the Surgery of Trauma (EAST), and the Western Trauma Association (WTA) (30).

CNTR's membership and the participation of members of national trauma organizations is a critical success factor in the NTRR. The CNTR Steering Committee includes representatives from each organization within CNTR and the DoD, and is focused not only on the development of NTRR, but also the development of a unified national trauma research agenda that establishes priorities and eliminates redundancies, a robust trauma research infrastructure that includes a Trauma Clinical Trials Network, and consistent and significant federal funding for research that increases the understanding of injury and informs clinical practice. In 2015, CNTR held its first Trauma Research Advocacy Day in Washington, DC, when 40 trauma surgeons traveled from across the United States to visit with key congressional contacts. This resulted in the addition of $10 million to the FY 2016 DoD budget, specifically to supplement DoD's efforts for the establishment of a National Trauma Clinical Trials Network. CNTR returned to Washington, DC in 2016 to request further funding to supplement DoD efforts in

support of the research network, again with a similar number of trauma surgeons so that its message reached the greatest number of key House and Senate members.

A collaborative approach, utilizing the experience and expertise of study investigators, is the most productive method of data-sharing to ensure reliability and quality of the manuscripts produced. CNTR is leveraging the expertise within ACS COT, DoD, data coordinating centers and research leaders from recent trauma multi-institutional randomized clinical trials such as the Glue Grant, ROC, and METRC. Even with the inherent challenges of developing a data-sharing platform, the generation, dissemination, and sharing of research data are key ingredients in contributing to scientific progress and the public good (29). The NTRR is an important piece of CNTR's knowledge translation plan, which encompasses robust dissemination of research outcomes via traditional and emerging channels, powerful new measurement tools that follow and gauge qualitative as well as quantitative uptake of information across sectors and platforms, and finally, review and synthesis that enable translation of knowledge into evidence-based practices. As planning and implementation steps continue, CNTR is committed to the rigorous and transparent development of NTRR in a way that involves the leaders and representatives of the national trauma research community.

CONCLUSION

Three components of a national approach to advance trauma care through research are a national research agenda, a trauma clinical trials network, and a research data repository. Clearly, these components require sustained funding at the federal level. Annual congressional special interest funds are short-term solutions to the problem, do not address the scope and impact comprehensively, and are meant to address or initiate one or two key and urgently needed capabilities for DoD/civilian sectors. Military-relevant trauma research has no safety net. It is a well-known phenomenon that as combat operations winds down after a conflict, combat casualty care research funding declines drastically (31). Civilian trauma care research needs cannot be met over the long term, as DoD priorities fluctuate over time. Additionally, research focused on several key patient populations and some injury treatments would likely never by funded by the DoD, e.g., research for the care of injured pediatric and geriatric populations.

A National Trauma Research Action Plan (NTRAP) supported by both Congress and the White House is essential to a mid-term strategy. This could be modeled in part after the National Research Action Plan (NRAP), which was issued as an Executive Order in 2013 to address improving access to mental health services for veterans, service members, and military families (32). NTRAP would require no appropriation and may be a plank for a future administration's platform for national healthcare.

The longer term solution for the country in this topic area is an enduring asset provided through a National Institute of Trauma supporting a National Clinical Trauma Research Program. This solution requires widespread public support and a congressional act that would insure that planned, programmed, and coordinated research occurs and the problem of trauma injury in America is finally addressed. In the meantime, NTI and CNTR will develop a robust NTRR and technology-driven knowledge translation plan to meet the current needs of trauma research community to leverage and make the most of the limited research funding available today.

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Impact of Department of Defense Funded Research at the

NATIONAL TRAUMA INSTITUTE

Funding Research ■ Changing Practice ■ Creating Awareness

Disclosure

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The opinions or assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the view of the Department of the Army or the Department of Defense.

Management of Blunt Abdominal Trauma and Splenic Injury

- First casualty Masirah Island Oman 30 Sep 2001
- ATV crash, unknown TOI, LOC, handlebar sign to LUQ abdomen
- iStat Hgb 12 and stable, no peritonitis
- FAST trace fluid in the pelvis
- Serial observation (12 ground transport, no CT scanner, no fluoro, no REBOA, warm fresh whole blood on the hoof)
- 3 day hospital LOS, serial outpatient f/u, stayed in deployed environment

Splenic Injury Prospective Outcomes Trial: An American Association for the Surgery of Trauma Multi-Institutional Study

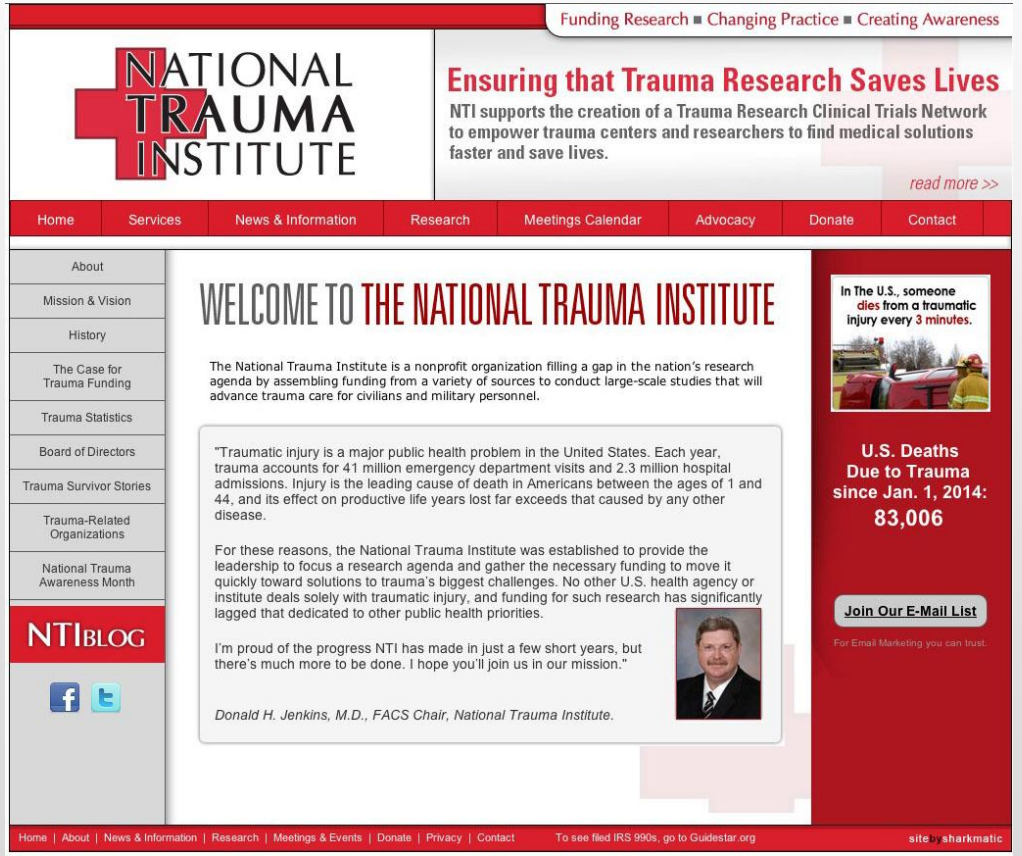
- Principal Investigator: Ben Zarzaur, MD, MPH at University of Tennessee Health Science Center
- First multi-institutional, long-term prospective study of patients with blunt splenic injury
- Funded by the DoD through the National Trauma Institute for $299,422 (NTI-NCH-10-020 & W81XW-11-1-0841)
- Results presented as AAST Plenary Paper in 2014 and published in the J of Trauma Acute Care Surgery in 2015 (Vol 79;3, 335-342)

Impact on the management of blunt splenic injury

- After the first 24 hour of nonoperative management, risk of splenectomy is rare:
  - 3.1% during inpatient phase of care
  - 0.27% during 180 days after discharge
- The benefits of splenic preservation techniques (angiography and embolization) are unclear. This study highlighted the need for further large scale multicenter trials that randomize to either management with angiography and embolization or nonoperative management.

National Trauma Institute Mission

- To generate funds for clinical trauma research
- To discover new funding opportunities
- To advocate for trauma research across federal entities as well as other agencies
- To distribute those funds to clinical investigators, but to do no research ourselves



National Trauma Institute Origins

NATIONAL TRAUMA INSTITUTE

- 2003: Began as local organization of 3 Level 1 Trauma Centers (TRISAT); based within University of Texas Health Science Center at San Antonio
- Product of both civilian and military trauma centers
- 2003-2006: Worked within UTHSCSA to achieve earmarks/federal appropriations
  - $4.2M total awarded for local trauma research/education & training; recruitment of first civilian burn center director at BAMC, funding salary for 5 years
- 2006: Reorganized as national non-profit entity
  - New Mission: to address lack of federal trauma research funding
  - New Leadership: National Board of Directors

NTI Board of Directors includes members of…

- American Association for the Surgery of Trauma
- Eastern Association for the Surgery of Trauma
- Western Trauma Association
- Shock Society
- American College of Emergency Physicians
- Orthopedic Trauma Association
- American Association of Neurological Surgeons
- US Army Institute of Surgical Research
- US Navy
- US Army
- US Air Force

NTI Research Priorities

- Hemorrhage
  - Non-compressible (truncal/torso)
  - Blood Products
  - Resuscitation
  - Shock and bleeding
  - Coagulopathy
  - Systemic and local hemostatic therapy
- Airway and Ventilation
- Infection
  - Eliminating hospital acquired infections in the ICU
  - Antibiotic utilization
- Disaster Preparedness
  - Mass casualty
  - Transportation of the critically ill
- Burn
  - New skin
  - Off the shelf skin
- Technology development

NTI Trauma Studies Funding Rounds

FIRST

- Issued first Request for Proposals (RFP) October 1, 2009 with $1.4M available funds
- 85 pre-proposals
- 15 full proposals reviewed on February 5, 2010
- 7 selected for funding March, 2010

SECOND

- Issued second RFP June 10, 2010 with $2.46M available funds
- 92 pre-proposals
- 21 full proposals reviewed on August 30, 2010
- 9 selected for funding January, 2011

NTI Funded Studies

16 Lead Sites

43 Participating Sites

NTI Research in 35 cities in 22 states

Funded Awards

PI Name	Institution	Study	$ Awarded	Participating Sites
Martin Croce	UTenn HSC	Multicenter Prospective Evaluation of the Ventilator Bundle in Injured Patients	$225,000	5
Joel Baseman	UTHSC - San Antonio	*Mycoplasma Pneumoniae* in the ICU	$190,000	5
Fred Pieracci	U Co. Denver	A Multicenter, Randomized, Double-blind Comparison of Intravenous Iron Supplementation to Placebo for the Anemia of Traumatic Critical Illness	$188,541	3
Shahid Shafi	Baylor Hosp, Dallas	Comparative Effectiveness of Clinical Care Processes in Resuscitation and Management of Moderate to Severe Traumatic Injuries	$225,000	3
Jason Sperry	U. Pittsburgh	Characterization of the Effects of the Early Sex-Hormone Environment Following Injury	$225,000	Single Center
Mitchell Cohen	UC-SF	Timing and Mechanism of Traumatic Coagulopathy	$225,000	2
Carrie Sims	U. Penn.	Vasopressin Supplementation during the Resuscitation of Hemorrhagic Shock	$125,000	Single Center
Ben Zarzaur	AAST/PI: UTenn HSC	Splenic Injury Prospective Outcomes Trial	$299,422	11

Funded Awards (continued)

PI Name	Institution	Study	$ Awarded	Participating Sites
Jay J Doucet	UC San Diego	Detection and Management of Non-Compressible Hemorrhage by Vena Cava Ultrasonography	$230,000	3
Jean-Francois Pittet	U AL Birmingham	Effect of Antioxidant Vitamins on Coagulopathy and Nosocomial Pneumonia after Severe Trauma	$300,000	Single Center
Mark Cipolle	Christiana HCS, DE	The Safety and Efficacy of Platelet Transfusion in Patients Receiving Antiplatelet Therapy that Sustain Intracranial Hemorrhage	$130,500	Single Center
Henry Cryer	UCLA	Transfusion of Stored Fresh Whole Blood in a Civilian Trauma Center: A Prospective Evaluation of Feasibility and Outcomes	$200,000	Single Center
Suresh Agarwal	Boston Med Center	Acute Lung Injury Ventilation Evaluation (ALIVE) Trial	$295,172	5
Robert Maxwell	UTenn HSC, Chattanooga	Methicillin-Resistant Staphylococcus aureus in a Trauma Population: Does Decolonization Prevent Infection?	$180,000	1
Martin A Schreiber	Oregon Health & Science University	Thrombelastography (TEG®) based dosing of enoxaparin for thromboprophylaxis: a prospective randomized trial	$675,761	3
Lena M. Napolitano	U Mich Health System, Ann Arbor	Hepcidin and Anemia in Trauma	$154,109	Single Center

Initial Scientific Contributions

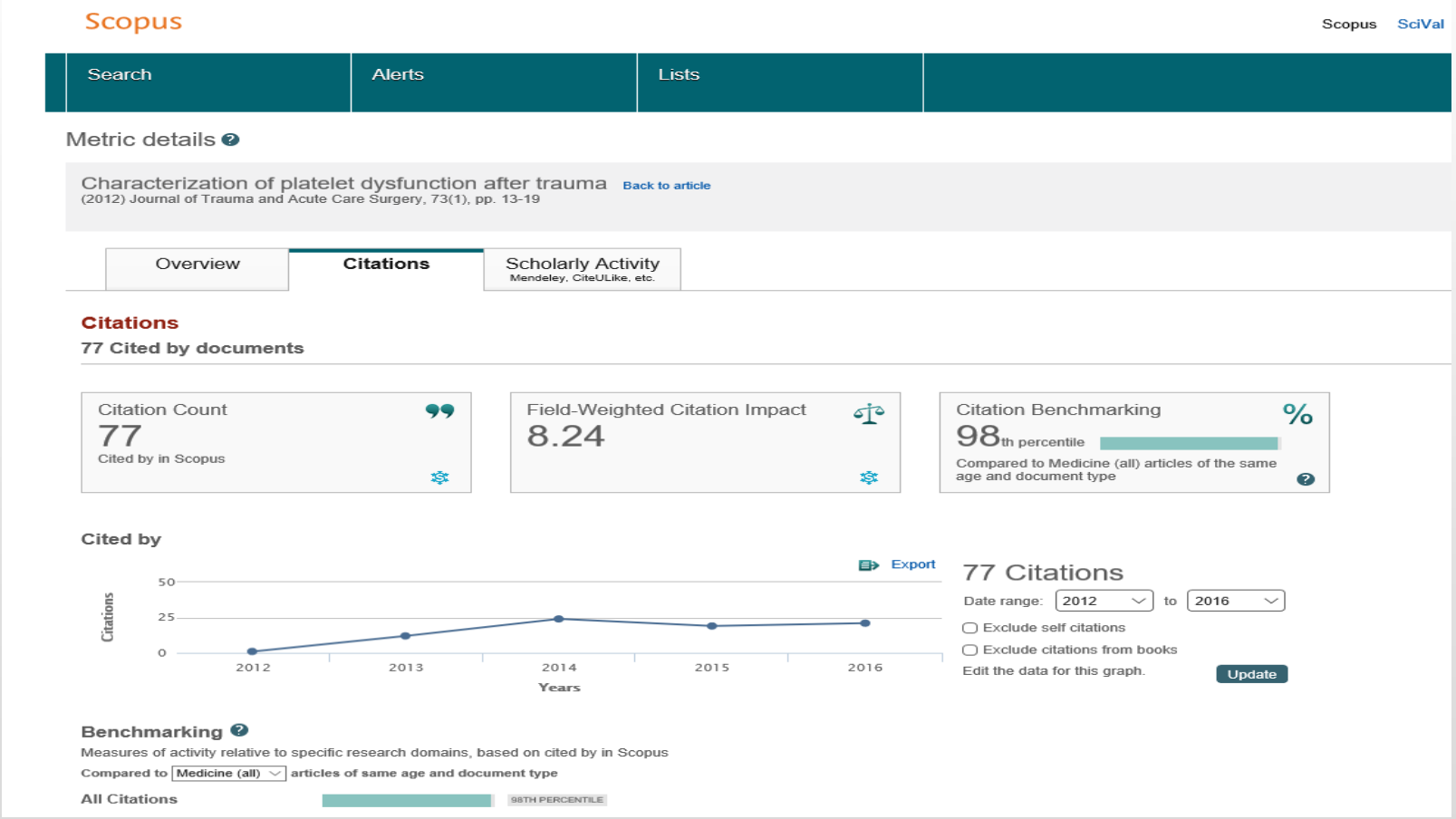
- Sixteen peer-reviewed publications
- Two publications in press
- One manuscript submitted/under review
- Sixteen national, 2 regional and 6 local presentations
- Ten of the 13 completed studies have published or submitted a manuscript (76%)
- Two PIs received additional funding through NTI applications to the Joint Warfighter Medical Research Program ($500K each)
- Twelve PIs trained junior researchers, fellows, residents or students on their study

Timing and Mechanism of Traumatic Coagulopathy

- Principal Investigator: Mitchell Cohen, MD, at University of California San Francisco
- Funded by the DoD through the National Trauma Institute for $224,950 (W81XWH-10-1-0924 & NTI-TRA-09-034)
- Prospective, multi-institutional observational study to characterize coagulation parameters in the severely injured, to use systems biology to identify the central mediators involved in coagulopathic phenotypes and to develop a predictive model to support diagnosis and treatment

Timing and Mechanism of Traumatic Coagulopathy (PI: Mitchell J. Cohen, MD)

The most cited publication from this study is the 2013 *JOT* manuscript *Characterization of platelet dysfunction after trauma*. It has been cited 77 times.



The Science of Conducting Trauma Research

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- Smith SL, Price MA, Fabian TC, Jurkovich G, Pruitt BA, Jr., Stewart RM, Jenkins DH. The National Trauma Research Repository: Ushering in a new era of trauma research. SHOCK: 2016 Military Supplement. Accepted for publication.

National Trauma Research Repository

- A robust, well-utilized and scalable repository for data resulting from current and future clinical trauma research
- All federally funded clinical trauma investigators will be eligible to contribute their data.
- Coordination between agencies and civilian academic and professional trauma organizations will further utilization, cooperation and collaboration.

10 Years of Advocating for Trauma Research

- Works with Congressional offices to seek sponsors and supporters to augment the Defense Health Agency budget for trauma research
- NTI works with principle investigators (PIs) and institutions to obtain funding through a competitive proposal process
- NTI has generated and/or managed $55M in trauma research funding since 2003

Coalition for National Trauma Research (CNTR)

- In 2014, CNTR formed to advocate for adequate, sustained federal funding for trauma clinical research studies and infrastructure
- CNTR successfully advocated for additional $10M in DoD budget for FY2016 for a clinical trauma research network
- Advocating for additional $10M in the DoD budget for FY2017 (supported by 15 senators and 69 representatives from a total of 25 states or 10% of both houses)
- Received notification of first DoD award to CNTR for *Multi-institutional Multidisciplinary Injury Mortality Investigation in the Civilian Pre-Hospital Environment (MIMIC*) to investigate potentially preventable deaths in the prehospital setting with 6 statewide medical examiner offices, the National Association of Medical Examiners and Johns Hopkins Bloomberg School of Public Health

NATIONAL TRAUMA INSTITUTE

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National Trauma Institute

National Trauma Research Repository Requirements Definition

NTRR
v1

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NTRR v1
Requirements Definition

Project Overview

NTRR will be the central repository for the clinical data resulting from both military and civilian federally funded trauma research and will be a web-based application with a user-friendly interface to contribute and access data. The data repository will assign unique identifiers, enabling data to be associated with a subject without personally identified information, provide functionality for queries and reports, and provide a common data dictionary so that data is consistently captured and recorded across trauma studies. The database may be housed at a federal agency such as DoD or NIH. The NTRR will have two major components. The Research Data Store (RDS) is for storing the data itself, in groups, packages, notebooks, bundles, or collections. The Research Data Catalogue (RDC) is for storing descriptions of the study data(Unique Data Elements (UDE) descriptions or study metadata), study protocols, data sharing plans and manuscripts.

Assumptions/Exclusions

Exclusions/assumptions are as follows:

- The system will be utilized to manage change for all areas within IT to include hardware, network, and software both purchased and internally developed.
- A Contributing Investigator (CI) is responsible for all the data generated during a single site or multisite study. If the CI is a sub-investigator (Site investigator) they have the authorization of the lead PI to register individually and upload data.

User Group Participants

The following user requirements are a collection of requirements reviewed and approved by the representatives listed below:

Name	Group
Donald Jenkins, Project Director	Project Principal Investigator
Michelle Price	NTI Quality Assurance

Key Definitions

Term	Definition
Contributing Investigator (CI):	A Contributing Investigator (CI) is the investigator (preferably the project Principal (Lead) Investigator (PI)) and is responsible for all the data generated from the study. Should the CI want to allow sub-investigators (site investigators) access to the data, the CI will specify at the time of study registration sub-investigators permissions (Read-only, Read-write (Upload), Edit, or Delete).
Contributing Coordinator (CC):	Assigned by the CI to have access for Read-Write (Upload) and Edit but not Delete.
Recipient Investigator (RI):	A Recipient Investigator will be any investigator querying the Research Data Catalogue (metadata) or requesting study data from the Research Data Store (RDS) from the repository for any purpose except as federal oversight or administrative action.
NTI Staff (NS) –	Managing users, processing Research Data Store (actual study data) requests (including forwarding the requests to the appropriate review committee), generating reports on the content of NTRR and the use requests.
DoD – contract oversight	DoD contracting officers will provide project oversight. DoD personnel will require access to Research Data Catalogue (study metadata) for reports.
General Public	Complete access to Research Data Catalogue. No access to the Research Data Store.

See also Data Dictionary.

System Requirements (Non-Functional)

Non-functional requirements are found below:

SR.1 System access must not require client-side installation.

SR.2 System must be scalable for increased user activity and storage capacity.

SR.3 System must provide a training system that mimics the actual production system.

SR.4 System should track active CDEs/UDEs vs inactive UDEs vs unstructured data for each study

Performance Requirements

Performance requirements are found below:

PR.1 System must be able to register, validate, track, authorize levels of access (e.g., a Principal Investigator registering as a CI may authorize levels of access for Sub-Investigators/coordinators) authenticate, and reset passwords.

1.1 The system shall allow user to create profile (register) and set credentials. Registration to include at a minimum the following information:

1.1.1 Date:
1.1.2 Type of Application: New; Renewal
1.1.3 First Name:
1.1.4 Last Name:
1.1.5 Middle Initial:
1.1.6 Degree:
1.1.7 Academic Position (or Title):
1.1.8 Institution:
1.1.9 Department:
1.1.10 Street Address:
1.1.11 City:
1.1.12 State/Province:
1.1.13 Zip/Postal Code:
1.1.14 Country:
1.1.15 Telephone:
1.1.16 FAX:
1.1.17 E-mail Address:

1.2 The system will track users: active (number of searches/filters in last year), inactive over one-year (period of time), roles: Contributing Investigator: CI; (CI-PI, CI-Sub-I, C-Coordinator) Recipient Investigator: (RI-PI, RI-Sub-I, R-Coordinator); contributor metrics (number of uploaded data sets), recipient metrics (number of downloaded data sets) and assigned Levels of Access per **PR.1**

1.2.1 Levels of access include:
1.2.1.1 Read-only
1.2.1.2 Read-Write/Upload
1.2.1.3 Read-Write-Edit
1.2.1.4 Read Write-Edit-Delete

1.3 The system shall authenticate user credentials (e.g., Shibboleth, OpenID (custom), OpenID Google, an internal table-based authentication method).

1.4 The system must contain an auto-logout setting

1.5 The system shall allow user to update the profile information and reset password.

PR.2 System must be able to require Log-on when applicable

2.1 Require registration and log-on only when querying/filtering data, requesting to upload or download data.

2.1.1 Research Data Catalog will be searchable

2.1.2 Basic reports on metadata for studies
2.1.3 Filters/queries should be able to combine filter by study metadata and filter by study fields.

PR.3 System must be able to tolerate multiple users querying Research Data Catalogue simultaneously and maintain a reasonable response time.

PR.4 The system shall support multiple roles for users (i.e., user can be both a CI and RI).

PR.5 The system shall support the ability for users to be affiliated with different studies.

PR.6 System must be able to work from external sources from a web based interface.

PR.7 System must be able to store applicable CDEs (See Data Dictionary).

PR.8 Description of each CDE variable fields include:

8.1 CDE ID
8.2 CDE Name
8.3 Variable Name
8.4 Definition / Description
8.5 Question Text
8.6 Permissible Value
8.7 Description
8.8 Data Type
8.9 Instructions
8.10 References
8.11 Population
8.12 Classification (e.g., Core)
8.13 Version #
8.14 Version Date
8.15 Aliases for Variable Name
8.16 CRF Module / Guideline
8.17 © or TM
8.18 Sub-Domain
8.19 Domain
8.20 Previous Title
8.21 Size
8.22 Input Restrictions
8.23 Min Value
8.24 Max Value
8.25 Measurement Type
8.26 LOINC ID
8.27 SNOMED
8.28 caDSR ID
8.29 CDISC ID
8.30 Disease

User Requirements (Functional)

NTRR Stakeholders (SH):

SH.1. Contributing Investigators (CI) – register studies, upload, review, correct and amend study metadata files to the Research Data Catalogue; and upload, review, correct and amend study data in the Research Data Store,.

SH.2. Contributing Coordinators (CC)- register studies upload, review, correct and amend study metadata files to the Research Data Catalogue; and upload, review, correct and amend study data in the Research Data Store as permitted by CI.

SH.3. Recipient Investigators (RI) – reviewing study metadata in the Research Data Catalogue for data available on the NTRR, request study data from Research Data Store

SH.4. NTI Staff (NS) – managing Research Data Store and Research Data Catalogue, managing users, processing data requests for data (including forwarding the requests to the appropriate review committee), generating reports on the content of NTRR (RDC and RDS) and the use requests, generating reports to CIs when their data are shared for secondary analysis

SH.5. DoD – NTRR project oversight

SH.6. General Public – review study metadata in Research Data Catalogue

User Requirements:

Requirement		Role			
		CI	RI	NTI	DoD
UR.1.	Should be able to manually map fields to existing CDEs/UDEs	x		x	
UR.2.	Should be able to upload data/files to the Research Data Catalogue and Research Data Store	x		x	
	i. Text data only	x		x	
	ii. In the future plan for images/video etc.	x		x	
UR.3.	Should be able to upload data from systems like MITC and REDCap	x		x	
UR.4.	Should be able to review their submitted data and change data when necessary	x		x	
UR.5.	Should be able to upload data dictionary and protocol	x		x	
UR.6.	Should be able to filter/query database and receive metadata results in a timely fashion (e.g., numbers of subjects that meet query criteria across multiple studies that met search criteria)	x	x	x	x
UR.7.	Should be able to request actual study data	x	x		x
UR.8.	Should be able to export data			x	
UR.9.	Administrator should be able to authorize access and permissions for NTI staff so that staff may:			x	
	i. Review/verify/approve registration requests			x	
	1. Request additional information on registrants			x	
	2. Verify registrants manually			x	
	ii. Map/import uploaded data to database manually			x	
	iii. Review/request additional information regarding uploaded data			x	
	iv. Approve/provide data for download requests and queries of the RDC			x	
	v. Run reports on the data in the RDS and RDC, numbers of studies, etc			x	

	vi. Track whether scheduled data submissions are timely (for ongoing NTI-affiliated studies)			x	
UR.10.	Should be able to save searches if logged in		x	x	x
UR.11.	System should be able to track the embargo status of data and provide reports to NTI staff, CIs, RIs and DoD	x	x	x	x
UR.12.	Run reports on the data on the registry, numbers of studies, numbers of data requests, embargo status of data (repository activity)			x	x

Reporting Requirements

The system shall be able to generate an "All Studies List" report

RR.AS.1. Report Objective

RR.AS.2. Report Title

- **i** "All Studies List"

RR.AS.3. Group Order and page break options

- **i** Order by Study Title

RR.AS.4. Selection Criteria (fixed or parameter driven)

RR.AS.5. Sort Order (ascending, descending, customized)

RR.AS.6. Report Summary if desired

RR.AS.7. Report Items (field names, calculated items)

- **i** Study Title;
- **ii** (Study metadata);
- **iii** CI-Names;
- **iv** RI-Names

RR.AS.8. Formatting (font type, size, date formats, lines or boxes, paper orientation)

RR.AS.9. Other Special Considerations

The system shall be able to generate an "Completed Studies List" report

RR.CS.1. Report Objective

RR.CS.2. Report Title

- **i** "Completed Studies List"

RR.CS.3. Group Order and page break options

ii Order by Study Title

RR.CS.4. Selection Criteria (fixed or parameter driven)

RR.CS.5. Sort Order (ascending, descending, customized)

RR.CS.6. Report Summary if desired

RR.CS.7. Report Items (field names, calculated items)

i Study Title;

ii (Study metadata);

iii CI-Names;

iv RI-Names

RR.CS.8. Formatting (font type, size, date formats, lines or boxes, paper orientation)

RR.CS.9. Other Special Considerations

The system shall be able to generate an "Open Studies List" report

RR.CS.10. Report Objective

RR.CS.11. Report Title

iii "Open Studies List"

RR.CS.12. Group Order and page break options

iv Order by Study Title

RR.CS.13. Selection Criteria (fixed or parameter driven)

RR.CS.14. Sort Order (ascending, descending, customized)

RR.CS.15. Report Summary if desired

RR.CS.16. Report Items (field names, calculated items)

i Study Title;

ii (Study metadata);

iii CI-Names;

iv RI-Names

RR.CS.17. Formatting (font type, size, date formats, lines or boxes, paper orientation)

RR.CS.18. Other Special Considerations

Requirements Definition Approval

A signature signifies the review and approval of the requirements defined in this document.

Task Area Manager **Signature**	**Date**	**Version**
		1.0

QA Chief **Signature**	**Date**	**Version**
		1.0

National Trauma Research Repository (NTRR) Use Cases

This document describes some of the ways that researchers and staff will interact with the National Trauma Research Repository (NTRR). The goal of the NTRR is to provide de-identified, well-described reusable data to foster collaboration, secondary analyses and data citations (not to mention meeting funding bodies' requirements). Below, we outline several different scenarios where various participants will interact with the NTRR.

The NTRR will have two major components. The Research Data Store (RDS) is for storing the data itself, in groups, packages, notebooks, bundles or "collections." The Research Data Catalogue (RDC) is for storing descriptions of the data (Common Data Elements (CDE) and Unique Data Elements (UDE) descriptions, protocols and study metadata). NTI is responsible for management of both components of the NTRR. In each case, there is a loop back from a NTI repository support team to the Researcher in the event that the data description needs to be improved to maximize its ability to advertise the existence of data, promote re-use and assist in data management.

It is interesting to note that: *Most data-management models map extremely poorly to the research-project cycles and timelines that researchers are accustomed to. The milestones researchers think about—grant applications, awards, data capture, data analysis, interim report writing, article authoring, renewal applications, and so forth—barely appear in data-management models.* In contrast, we are presenting use cases that correspond to institutional triggers, including grant applications and awards.

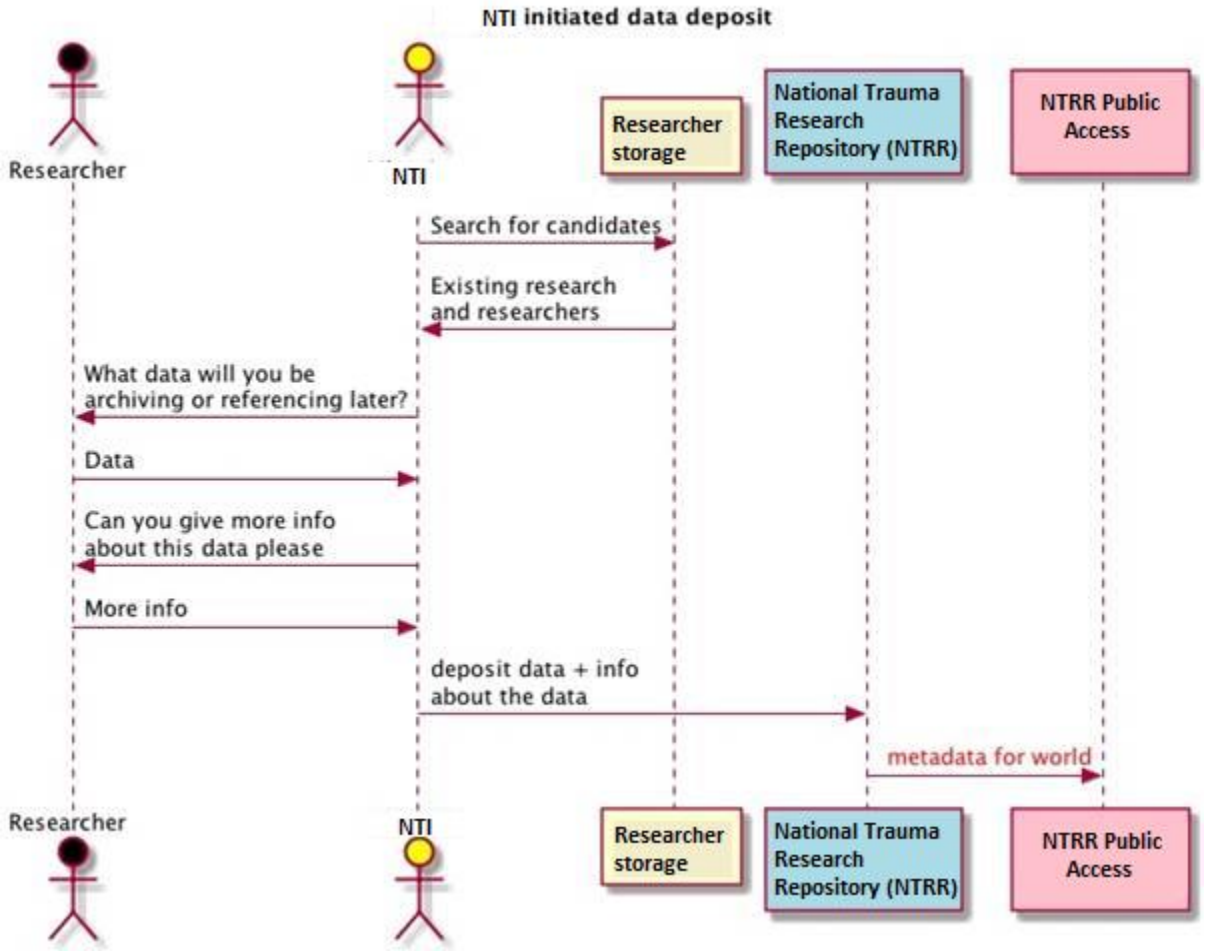
A WORD ABOUT THE DIAGRAMS

The diagrams in this document all have slightly differing levels of detail – the idea is to illustrate each point once, rather than repeat things. A few points to keep in mind when reading the diagrams:

- Research data and the methods for producing data come in all varieties. The diagrams are necessarily simple, so as not to exclude data types or different ways of handling data.
- All diagrams represent use by Contributing Investigators (adding their data to NTRR) except the last diagram, which represents use by Recipient Investigators (requesting/receiving data from NTRR for secondary analysis).

NTI-led Deposits

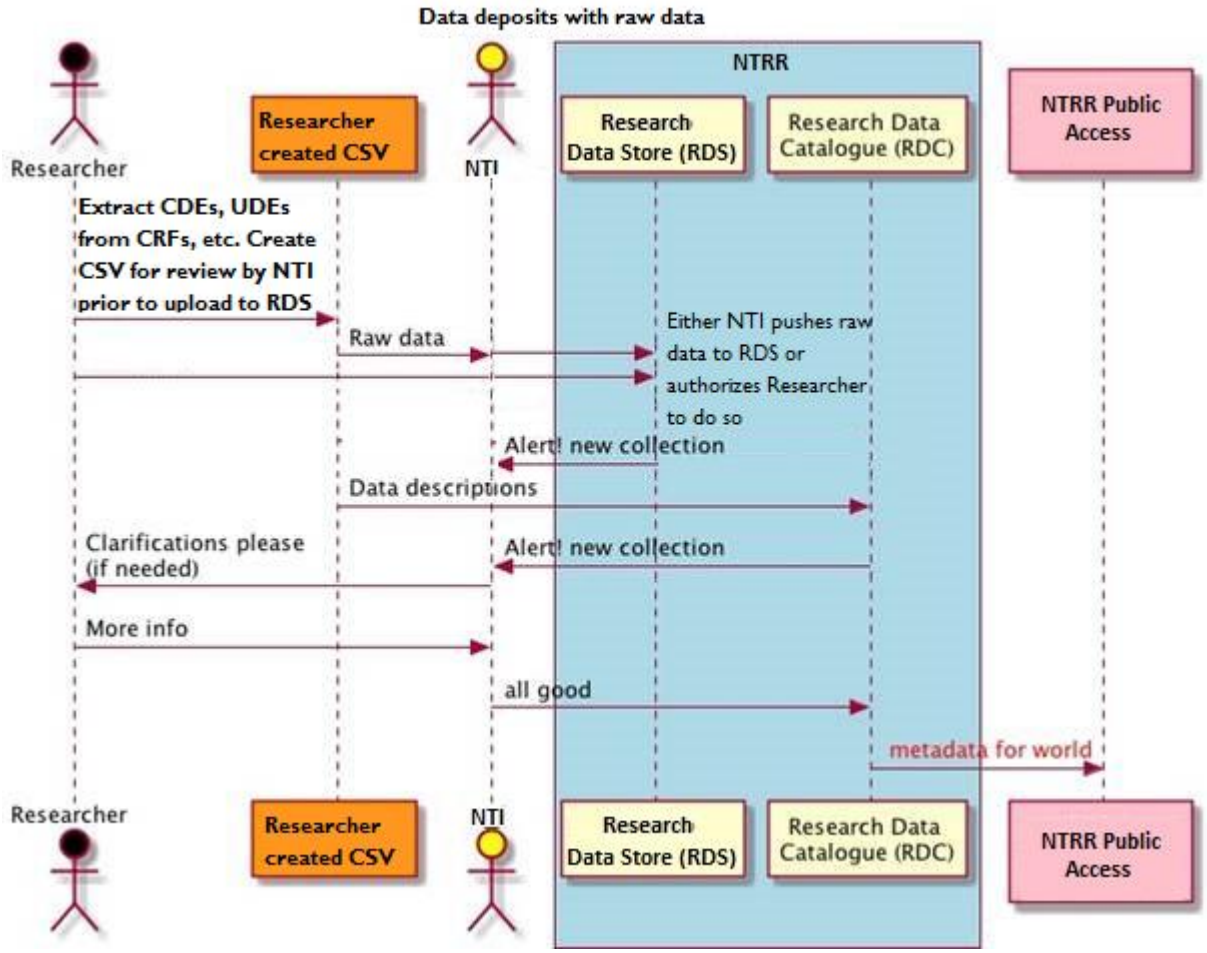
The first use case, NTI-led deposits, deals with historical research completed some time ago, research that has recently completed, or research that is ongoing but has been flagged as a potential candidate for inclusion in the repository for strategic reasons. This project involves the NTRR support team identifying places that relevant trauma data reside via discussions with research administration and evaluating NTI's completed study datasets for possible inclusion.



Data Capture Deposits

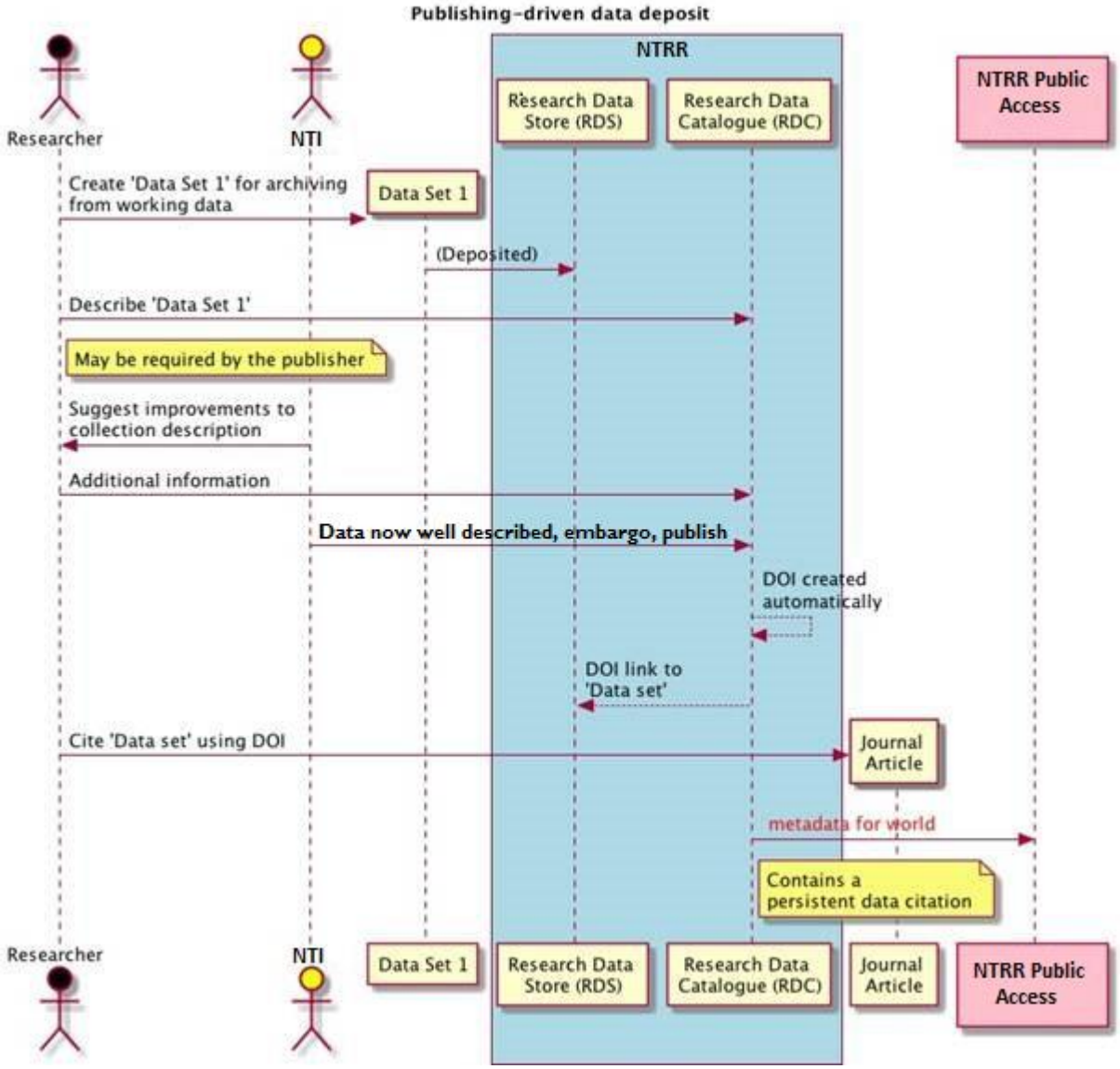
A lot of research data are generated by machines such as sensors or instruments in such a way that it can be captured, labelled and described close to the data source. We don't currently have

any automated data capture projects; however, the plan would be to house those in a working data store. For some other scenarios, particularly compiling a data set to support a publication (which is covered below), NTI staff will be involved in selecting and describing data. There is an additional level of detail in this diagram, which is not in the NTI-led process above, which simply makes explicit the fact that the NTRR encompasses the storage and the catalogue. The storage is where data are deposited, and the catalogue is where the descriptions of the data are kept.



Publishing/citation-driven Deposits

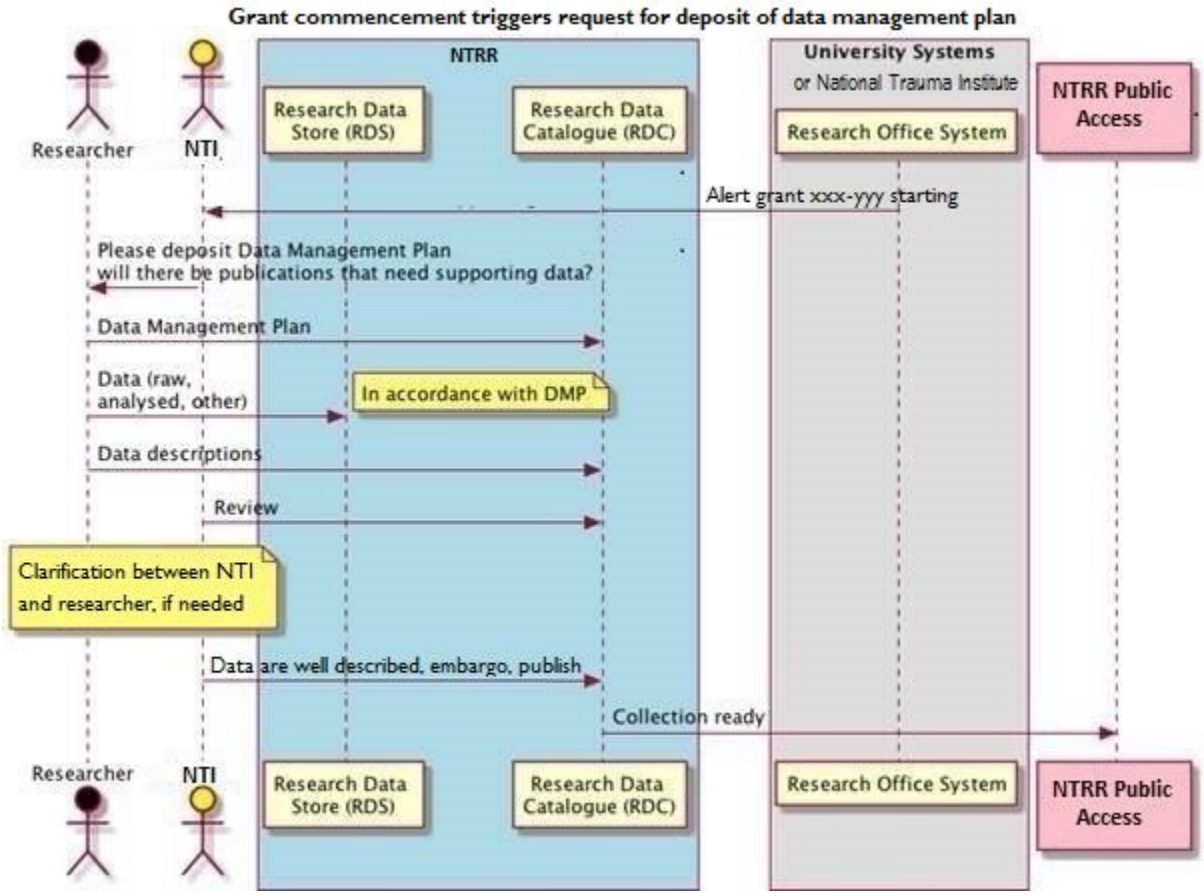
We have been approached by researchers wanting to deposit data somewhere accessible because it is required by the journal to which they're submitting. This will become more important as funders start to mandate open access data along with open access publications. Note that in this scenario there is a DOI – a Digital Object Identifier – created for a data set so it can be cited like a publication.

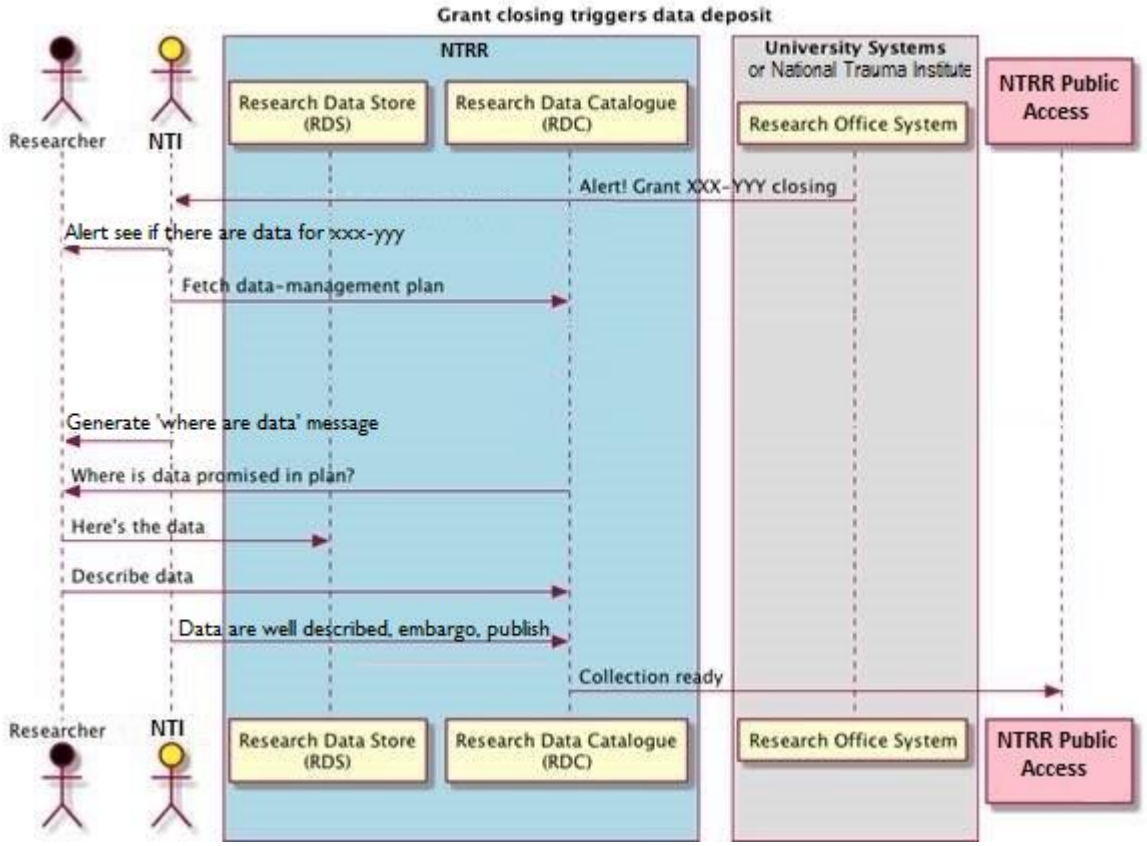


Grant-driven Data Deposits

Grants are key to the research lifecycle. Work has already been done on integrating data management into the research lifecycle, starting with applications for internal grants. We know that changing the research culture will take some time, but eventually thinking about eResearch requirements--not just data management but computing and collaboration needs--will become normal for all researchers, just as ethics forms are normal for many now.

We present two scenarios here: one when a grant starts, and the researcher is prompted to finish and deposit a data management plan; and another when the grant finishes, and there is a check to make sure the data management plan has been followed. In between, of course, there might be other research-lifecycle events that trigger data deposits.

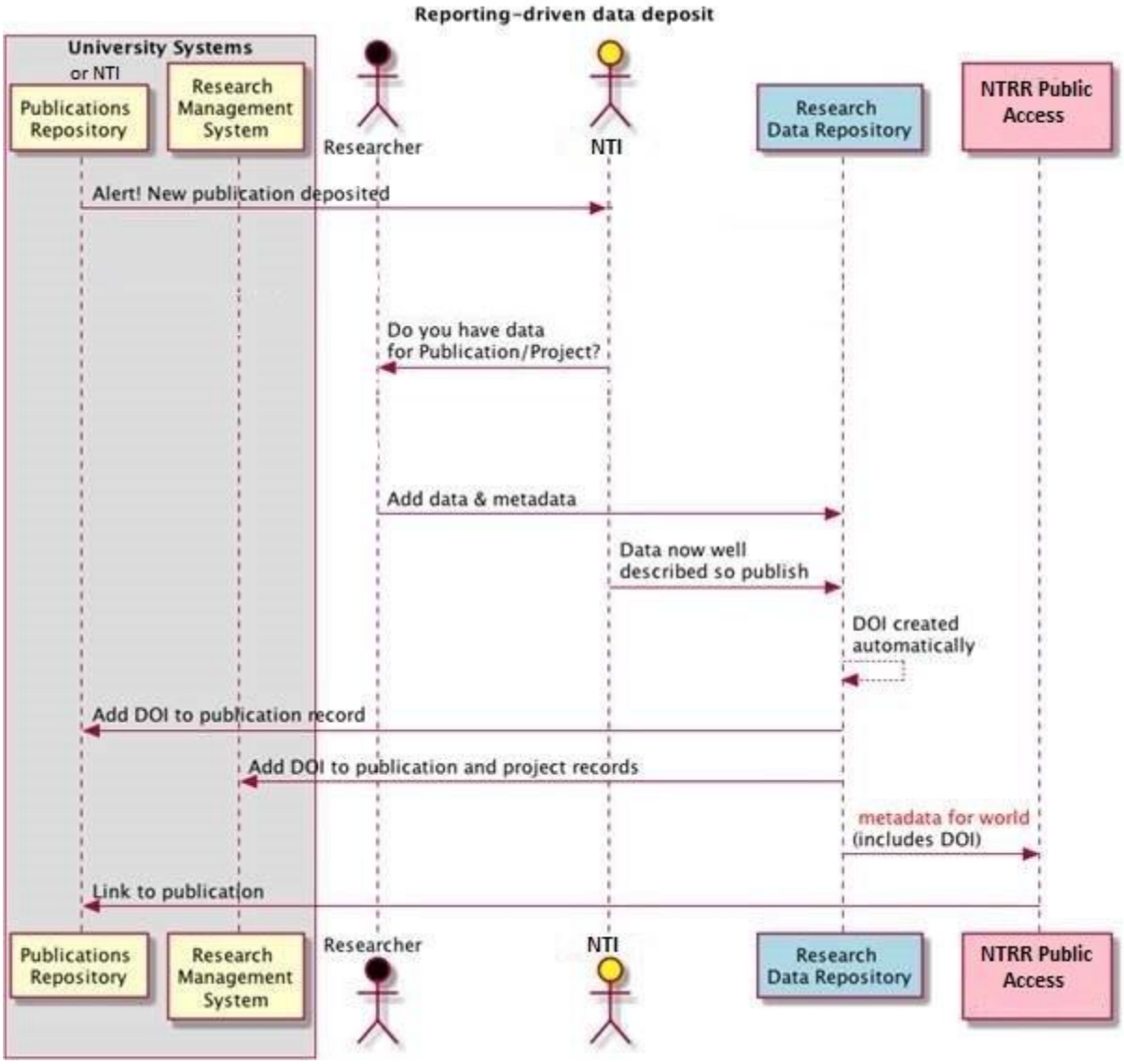




Reporting-driven Data Deposit and Output Capabilities

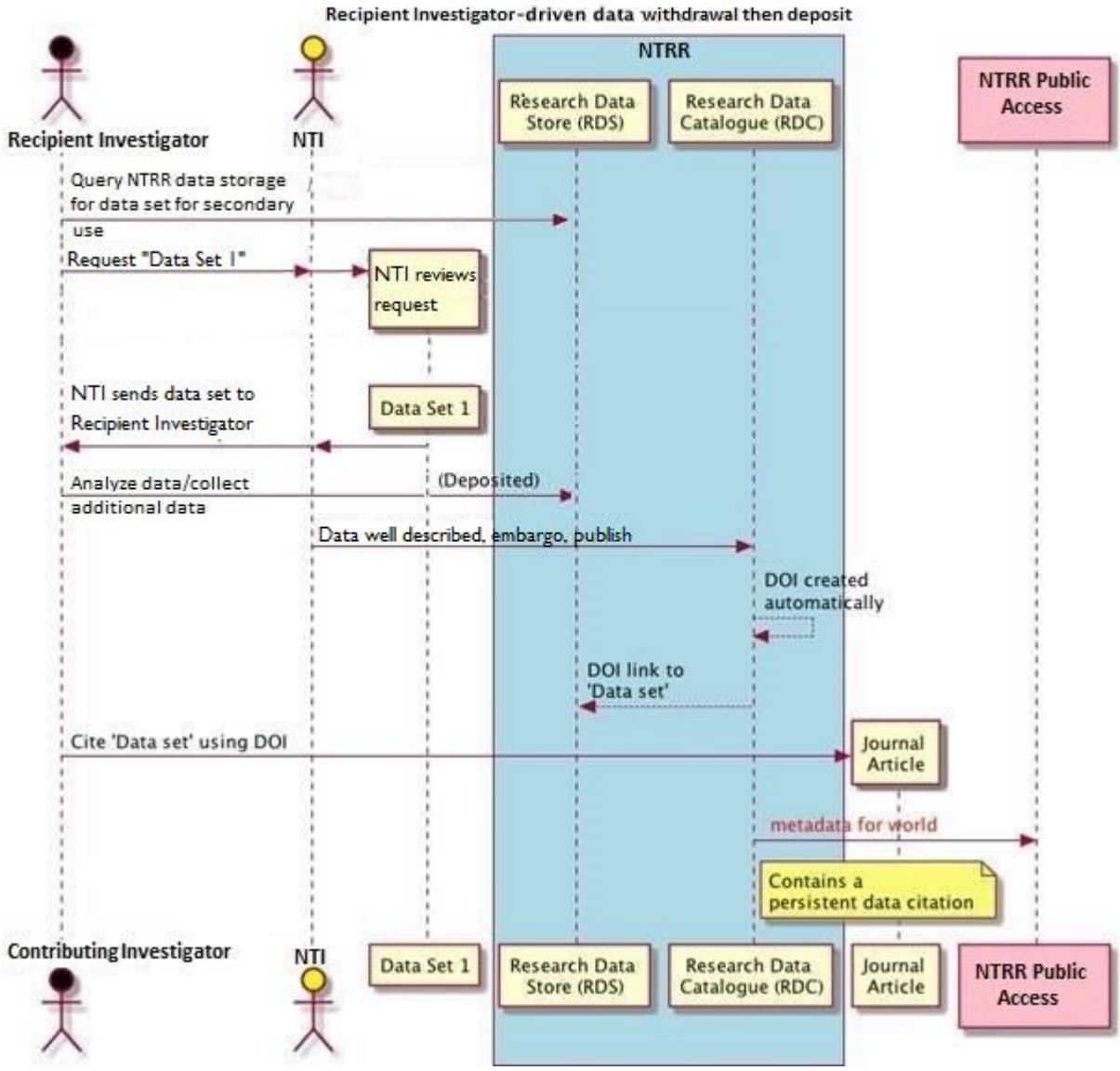
All universities have to report on publications, and this means that there are processes in place for reporting that form a large part of the research lifecycle. This is another place to tie-in data management processes for data that is of strategic significance. The next diagram shows a couple of scenarios that could be driven by the reporting cycle: either a significant publication, where it is important to make sure that data is kept for reproducibility and reuse, or when reporting on research of global significance, where advertising data might lead to more such research.

Additionally, contributing investigators, NTRR staff and funding officers will need to generate reports from NTRR on the number of subjects enrolled in ongoing studies, the total number and types of studies contributing data to NTRR. Contributing investigators will also receive reports on recipient investigators who have requested their data to facilitate collaboration.



Recipient Investigator-driven Data Withdrawal

Recipient investigators will access the NTRR public site to query the Research Data Catalogue for data available for secondary use. They will submit a formal data request that will be reviewed and approved by NTRR. NTI staff will generate and send the dataset to the recipient investigator. The recipient investigator may add to the data set, though this is unlikely, given its de-identified structure. The recipient investigator will then analyze their data, which includes a withdrawal of Data Set 1 from the repository and possibly the collection of additional data. As part of their data management plan, Recipient Investigators will become Contributing Investigators when they deposit their data set as a new study relying on NTRR.



National Trauma Research Repository (NTRR)
Policy on Policies

Table of Contents

I. Policy

A. All NTRR written policies and procedures (collectively referred to as policy) will be written based on all available, applicable federal, state and local laws, regulations and policies.

B. All NTRR written policies will be written using the attached template for policies and procedures

C. All written policies will be certified as active only after review by the NTRR Manager/PI and input of all applicable entities, appropriate NTI officials and NTRR committee or subcommittees when necessary.

D. All new and revised policies and procedures and other NTRR guidance will be posted to the NTI/NTRR website for use by the research community.

II. Overview

A. This procedure starts upon creation of or modification of a specific NTRR policy

B. This procedure ends when the specific NTRR policy is activated.

C. Summary of responsibilities

1. NTRR Manager is responsible for researching, drafting, modifying proposed and existing NTRR policies.

2. The NTI support office of the NTRR (NTI) staff is responsible for researching, drafting, modifying proposed and existing NTRR policies at the discretion of the NTRR Manager/PI.

III. Procedure

A. The proposed or existing NTRR policy is scheduled for creation or modification by the NTRR Manager/PI

1. The NTRR Manager or NTRR PI

a) researches, drafts, modifies the policy, or;

b) assigns personnel to research, draft, or modify the policy;

c) determines which policy requires input of which applicable entities, appropriate NTI officials or NTRR committee or subcommittees;

B. The NTRR Manager/PI, assigned NTI Staff or NTRR committee or subcommittees member(s) use the following references in drafting or modifying policy and procedures relating to:

1. Determination of What Activities are Human Research

    a) 21 CFR 56.102

    b) 38 CFR 16.102

    c) 45 CFR 46.102

    d) DoD Instruction (DoDI) 3216.02 Definition: research involving human subjects

2. Determination of What Data are De-identified

    a) 45 CFR 164.514 (a-d)

    b) 32 CFR 310 (set forth in DoD Directive 5400.11 and 5400.11-R Department of Defense Privacy Program)

        (1) 32 CFR 310.4(n) and DoD 540.11-R, DL1.14. Definitions of “Personal Information”

        (2) 32 CFR 310.22 “Non-consensual conditions of disclosure” specifically, examples of personal information regarding DoD civilian, federal civilian and Military Member employees that normally may be released and (e)(2) and DoD 540.11-R, C4.2.5. Disclosures for Statistical Research. “…The records shall be transferred to the requester in a form that is not individually identifiable…”

        (3) 310.24 Disclosures to the public from medical records.

    c) Applicable sections of DoD 6025.18-r, including:

        (1) C8.1. De-Identification of Protected Health Information.

3. Determination of What Data are Limited Data Sets

    a) 45 CFR 164.514 (e)

    b) Applicable sections of DoD 6025.18-r, including:

        (1) C8.3. Limited Data Set.

4. NTRR

    a) Concerning NTRR procedures

        (1) Applicable sections of 45 CFR 46 (e.g., 103(b)(4 and 5), 108)

        (2) Applicable sections of 21 CFR 56 (e.g., 108(c))

(3) Applicable sections of DoD 3216.02 (when DoD research is involved)

(4) Applicable sections of 38 CFR 16 (e.g., 108) when VA research is involved).

b) Concerning NTRR review and approval of contributing researcher data and requests from recipient researchers for data

(1) Applicable sections of The Belmont Report, Ethical Principles and Guidelines for the Protection of Human Subjects of Research, The National Commission for the Protection Of Human Subjects of Biomedical and Behavioral Research, April 18, 1979, for example:

(a) Page 4, item 3 “An injustice occurs when some benefit to which a person is entitled is denied without good reason or when some burden is imposed unduly.”

(2) Applicable sections of 21 CFR 50, for example:

(a) 21 CFR 50.25

(3) Applicable sections of 21 CFR 56, for example:

(a) 21 CFR 56.111

(4) Applicable sections of 38 CFR 16 when VA research is involved, for example:

(a) 38 CFR 16.109

(b) 38 CFR 16.111

(5) Applicable sections of 45 CFR 46, for example:

(a) 45 CFR 46.108

(b) 45 CFR 46.109

(c) 45 CFR 46.111

(d) 45 CFR 46.116

(e) 45 CFR 46.117

(f) 45 CFR 46 Subparts B

(g) 45 CFR 46 Subparts C

(h) 45 CFR 46 Subparts D & 21 CFR 50 Subpart D

(6) Applicable sections of DoDI 3216.02

(a) Part II. Definitions

(b) Enclosure 3, 2a. Activities for Which an Institution is Required to Have a Federal Assurance.

(c) Enclosure 3, 3. DoD-Conducted Research Involving Human Subjects

(d) Enclosure 3, 4. Research Involving Human Subjects Conducted by a Non-DoD Institution .

(e) Enclosure 3, 7. Additional Protections for Human Subjects

(f) Enclosure 3, 8. Research Monitor

(g) Enclosure 3, 9. Unique DoD Limitations On Waiver Of Informed Consent.

c) Concerning informed consent

(1) Applicable sections of 45 CFR 46, for example:

(a) 45 CFR 46.101(i)

(b) 45 CFR 46.109 (b),(c)

(c) 45 CFR 46.111

(d) 45 CFR 46.116

(e) 45 CFR 46.117

(2) Applicable sections of 21 CFR 50, for example:

(a) 21 CFR 50.20

(b) 21 CFR 50.23-25

(c) 21 CFR 50.27

(3) Applicable sections of 21 CFR 56, for example:

(a) 21 CFR 56.109 (b),(c)

(4) Applicable sections of 38 CFR 16 (e.g., 116, 117) when VA research is involved, for example:

(a) 38 CFR 16.116

(b) 38 CFR 16.117

(5) Applicable sections of Title 38 USC 1710(f) and 1710(g)

(6) Veterans Health Administration Handbook 1200.5 34 CFR 97 [Department of Education Subpart D]

(7) Specifically concerning Waivers of Consent

(a) A waiver, by an IRB, of informed consent for the research, in accordance with 10 CFR 745.116(d), 14 CFR 1230.116(d), 15 CFR 27.116(d), 16 CFR 1028.116(d), 21 CFR 50.24, 22 CFR 225.116(d), 24 CFR 60.116(d), 28 CFR 46.116(d), 32 CFR 219.116(d), 34 CFR 97.116(d), 38 CFR 16.116(d), 40 CFR 26.116(d), 45 CFR 46.116(d), 45 CFR 690.116(d), or 49 CFR 11.116(d)

(8) Applicable sections of DoDI 3216.02 concerning Waivers of Consent

(a) Enclosure 3, 9. Unique DoD Limitations On Waiver Of Informed Consent..

5. Complaints (Subject Complaints)

a) 45 CFR 46.116(a)

b) 21 CFR 50.25(a)

6. Coordination

a) No references for most committee coordination.

b) STVHCS

(1) 38 CFR 16

(2) Veterans Health Administration Handbook 1200.5

7. Conflict of Interest

a) 38 CFR 16.107(e)

b) 21 CFR 46.103, 107

c) 21 CFR 56.107

d) 21 CFR 54 (as reference)

e) 42 CFR 50 Subpart F

f) OHRP May 2004 Financial Relationships and Interests in Research Involving Human Subjects: Guidance for Human Subject Protection

8. Cognitively impaired:

a) Federal regulations at 45 CFR 46.111(a)(3) require that NTRRs take into account the special problems of research involving vulnerable populations. There is no other explicit Federal or Texas statue that speaks to the inclusion of cognitively impaired subjects in research.

b) Veterans Health Administration Handbook 1200.5

9. Privacy and Confidentiality (See also HIPAA at III.B.23 below):

a) Federal regulations at:

(1) Applicable sections of 21 CFR 50 (e.g., 50.25(a)(5) “Elements of Consent” concerning How confidential records will be maintained, FDA may inspect)and 56 e.g., 56.111(a)(7) “Privacy and confidentiality will be protected”)

(2) Applicable sections of 21 CFR 812 (e.g., 812.38 “Confidentiality of data and information”)

(3) Applicable sections of 21 CFR 312 (e.g., 312.130(c) concerning release of an IND safety report relating to the use in the individual to the individual)

(4) Applicable sections of 45 CFR 46 (e.g., 46.102 Definitions of Human Subject, Identifiable private information and Private information; 46.111(a)(1)(7) under “Criteria for NTRR approval of research” concerning “When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data”; 46.116(a)(5) under Basic elements of informed consent “A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained” and 46.117(c)(1) under Documentation of Informed Consent “That the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality.”)

(5) 45 CFR 160 and 164 Privacy Rule (HIPAA)

(6) 32 CFR 310 (set forth in DoD Directive 5400.11 and 5400.11-R Department of Defense Privacy Program) and applicable sections of DoD 6025.18-r

b) State regulations at:

(1) Texas Health and Safety Code,

(a) Chapter 181 Medical Records Privacy

(b) Chapter 161 Public Health Provisions, 161.0073 Registry Confidentiality (Child immunization registry).

(c) Chapter 241 Hospitals, 241.151 Definitions.

(d) Chapter 241 Hospitals, 241.152. Written Authorization For Disclosure Of Health Care Information.

(e) Chapter 241 Hospitals, 241.153. Disclosure Without Written Authorization

(f) Chapter 611 Mental Health Records, 611.004. Authorized Disclosure Of Confidential Information

(g) Chapter 611 Mental Health Records, 611.0045. Right To Mental Health Record

(h) Chapter 773 Emergency Medical Services, 773.092. Exceptions

(i) Chapter 773 Emergency Medical Services, 773.093. Consent.

(j) Chapter 47 Hearing Loss In Newborns, 47.008 Confidentiality And General Access To Data

(k) Chapter 81 Communicable Diseases, 81.103 Definitions

(2) Occupations Code, Title 3, Chapter 159, "Physician-Patient Communication" including but not limited to:

(a) Sec. 159.002. Confidential Communications

(b) Sec. 159.004. Exceptions to Confidentiality in Other Situations. An exception to the privilege of confidentiality in a situation other than a court or administrative proceeding, allowing disclosure of confidential information by a physician, exists only with respect to the following: (2) medical or law enforcement personnel, if the physician determines that there is a probability of: medical or law enforcement personnel, if the physician determines that there is a probability of: (A) imminent physical injury to the patient, the physician, or another person; or (B) immediate mental or emotional injury to the patient; (3) qualified personnel for research.

(c) Sec. 159.005. Consent For Release Of Confidential Information.

c) Applicable sections of “Patient Privacy Policies” in Chapter 11 of the HOP including but not limited to:

(1) “Patient Health Records” in Section 11.1.5.

(2) “Confidentiality of Patient Health Information” in Section 11.1.6.

(3) “Uses and Disclosures of Protected Health Information” in Section 11.2.

(a) “De-identification of Protected Health Information” in Section 11.2.9.

(b) “Uses and Disclosures of Protected Health Information for Research” in Section 11.2.12.

10. Data Safety Monitoring

a) Federal Regulations at

(1) 45 CFR 46.111(a)(6) When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects. (DHHS)

(2) 38 CFR 16.111(a)(6) When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects. (VA)

(3) 21 CFR 56.111(a)(6) Where appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects. [Sponsors are required to monitor studies evaluating new drugs, biologics, and devices (see 21 CFR 312.50 and 312.56 for drugs and biologics, as well as 21 CFR 600.80, and 21 CFR 812.40 and 812.46 for devices).] (FDA)

(4) 32 CFR 219.111(a)(6) Where appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects. (DoD)

11. Exempt

a) 45 CFR §46.101(b)(1)-(6), 45 CFR §46.301(a), 21 CFR §56.104(c)-(d), OHRP Guidance

b) 45 CFR 46.101(b)(5): Exemption for Research and Demonstration Projects on Public Benefit and Service Programs,

c) OHRP Guidance on the Involvement of Prisoners in Research, May 23, 2003, Federal Register, Vol. 48, pp. 9266-9270, March 4, 1983

12. Continuation Review

a) 21 CFR 56.108(a)(1)&(2)

b) 21 CFR 56.109(f)

c) 21 CFR 56.110

d) 21 CFR 56.111

e) 21 CFR 56.115(a)(3)&(7)

f) 38 CFR 16.103(b)(4)

g) 38 CFR 16.108(b)

h) 38 CFR 16.109(e)

i) 38 CFR 16.110

j) 38 CFR 16.111

k) 38 CFR 16.115(a)(3)&(7)

l) 45 CFR 46.103(b)(4)

m) 45 CFR 46.108(b)

n) 45 CFR 46.109(e)

o) 45 CFR 46.110

p) 45 CFR 46.111

q) 45 CFR 46.115(a)(3)&(7)

13. Modifications and amendments

a) 21 CFR 56.110(b)(2)

b) 38 CFR 16.110(b)(2)

c) 45 CFR 46.110(b)(2)

d) 38 CFR 16.111

e) 45 CFR 46.111

f) 21 CFR 56.111

14. Expedited Review

a) 45 CFR 46.103(b)(4), 45 CFR 46.110(b), 45 CFR 46.110(c)

b) 21 CFR 56.108(a), 21 CFR 56.110(b), 21 CFR 56.110(c)

c) Human Subject Protections (Office for Protection from Research Risks (OPRR) Report) Number 93-01, November 9, 1992, Local NTRR Review of Multicenter Clinical Trials: Clarifying procedures for local IRB review of National Institutes of Health (NIH) multicenter Clinical Trials

d) OHRP Compliance Activities: Common Findings and Guidance #14, #15, #20, #26, #71(f),

e) OHRP Guidance on Expedited Review

f) FDA Information Sheets: Frequently Asked Questions: IRB Procedures,

g) FDA Information Sheets: Recruiting Study Subjects

h) Information Sheet Guidance for IRBs, Clinical Investigators, and Sponsors Significant Risk and Nonsignificant Risk Medical Device Studies Jan 2006.

i) Categories of Research That May Be Reviewed by the Institutional Review Board (IRB) through an Expedited Review Procedure – FDA & DHHS

j) NTRR policies and procedures, “Modifications and Amendments” Policy

k) NTRR policies and procedures, “Continuation Review” Policy

l) NTRR policies and procedures, “Informed Consent” Policy

m) 45 CFR 46.110

n) 45 CFR 46.102 (i)

o) 38 CFR 102(i)

p) 21 CFR 56.110

q) 21 CFR 56.102(i)

r) 38 CFR 16.110

15. Off Site Research

a) Office for Human Research Protections (OHRP)

(1) Engagement Memo

(2) Terms of the Federal-wide Assurance of Protection for Human Subjects

(3) IRB Knowledge of Local Research Context Guidance

(4) Sample Unaffiliated Investigator Agreement

(5) 45 CFR 46.114

b) Food and Drug Administration (FDA)

(1) Cooperative Research Guidance

(2) Non-Local IRB Review Guidance

(3) 21 CFR parts 50 and 56

16. Advertising

a) Guidance materials compiled from OHRP IRB Guidebook: Chapter IV, Consideration of Research Design, “Identification and recruitment of subjects”, FDA information sheet “Recruiting Study Subjects”

b) 21 CFR 50.20, 21 CFR 50.25, 21 CFR 56.111(a)(3), 21 CFR 56.111(b), 21 CFR 812.20(b)(11)

c) http://www.hhs.gov/ohrp/policy/clinicaltrials.html

d) http://www.fda.gov/oc/ohrt/IRBs/toc4.html#recruiting

e) HHS regulations at 45 CFR 46.109(b) require that IRBs ensure that information given to subjects as part of informed consent meets the requirements specified in the regulations at 45 CFR 46.116.

17. Records

a) Federal regulations at

(1) Refer to specific grant contract for record keeping requirements.

b) State and Local regulations are discussed in Policies which include:

(1) NTRR Records and Information Management and Retention Policy

(2) State of Texas Record Retention Schedule: Medical Services / Research and Development 130 DE. (AC +15 years)

(a) Grants Records - Grants which include clinical trials / drug studies. This records series consists of research data and documentation gathered or created in the course of a clinical trial. May include but is not limited to case history records, case reports, study protocol and amendments, patient care data, objectives and

purpose of the study, selection criteria, clinical procedures, FDA forms, serious adverse events reports, study design and other documentation relating to study protocols, pharmaceutical studies, findings, research papers, and serious adverse events reports.

(b) AC = After completion and upon receipt of notice of new drug application approval or investigational new drug withdrawal (21 CFR 312.57). Includes both federal and non-federal grants and sponsored agreements. Departments may keep text portions of grants and data compiled as long as they are deemed administratively valuable.

c) Record retention considerations include:

(1) Record retention regulations and guidance are dependent on funding source.

(2) Record retention for investigators requires consideration in drafting NTRR record retention requirements.

(3) NIH regulations- record retention is 3 years after the final financial report and includes: financial and programmatic records, supporting documents statistical records, and all other records that are required by the terms of a grant or may reasonably be considered pertinent to a grant for a period of 3 years from the date the annual FSR is submitted.

(4) NSF regulations also call for records to be retained for at least 3 years.

(5) FDA regulations:

(a) For IND applications:

(i) for 2 years following date a marketing application is approved for the drug for the indication being investigated;

(ii) OR until 2 years after the investigation is discontinued and FDA is notified that investigator does not plan to file for market application

(b) For non-clinical Lab study results for whichever period is shorter:

(i) 2 years following approval by FDA of the application for research or marketing permit which was filed. or

(ii) 5 years following date results of lab study submitted to FDA in support of application for a research or marketing permit or

(iii) 2 years following the date on which the study is completed, terminated, or discontinued if study does not result in submission of application for research or marketing permit

(6) HHS protection of human subject regulations require the institution to retain research records for at least 3 years after completion of research and either the institution or

the PI designated by the institution should also retain the informed consents signed by the subjects (hard copy or electronic) for at least 3 years after completion of the research.

(7) UCSF Brain Tumor Research Center developed detailed guidelines for research data and manuscripts in 1989 with a revision in 2000. These are recognized as comprehensive guidelines for responsible data management. They suggest PI store and retain records at least 5 years after ending of funding for study.

(8) Other considerations which might warrant longer retention of research data or supporting clinical information:

(a) Data sets which are not easily reproduced and might have significant secondary uses.

(b) Data that is widely recognized as having very unusual significance that is indeed unique.

(c) So in general if special considerations not a factor 3-5 years after study completed is usually sufficient.

(9) If investigators have been designated to retain certain records (e.g., informed consent documents signed by subjects) on behalf of the institution as required by the HHS regulations at 45 CFR 46.115(b), they must retain the records in some form. Such records may be preserved in hardcopy, electronic or other media form and must be accessible for inspection and copying by authorized representatives of HHS at reasonable times and in a reasonable manner (45 CFR 46.115(b)). Retention of multiple copies of each **record** is not required.

(10) If investigators who have been designated to retain records on behalf of the institution leave that institution, the investigators and the institution should identify the successor responsible for maintaining those institutional records, either at the original institution or wherever the records are relocated, for the period of time required under HHS regulations at 45 CFR 46.115(b).

(11) VA Handbook 1200.5, 7.j. **Record Retention.**

(a) The required records, including the investigator's research records, must be retained for a minimum of 5 years after the completion of the study and in accordance with VHA's Records Control Schedule (RCS 10-1), applicable FDA and DHHS regulations, or as required by outside sponsors.

(i) All records must be accessible for inspection and copying by authorized representatives of VA, OHRP, FDA and other authorized entities at reasonable times and in a reasonable manner.

(ii) Records are the property and the responsibility of the local research office. The medical center must designate where the records will be maintained and/or stored.

(iii) Complete (non-redacted) minutes, whether from the VA or affiliate NTRR reviewing VA research, must be submitted to the R&D Committee and maintained in the facility research office. The R&D Committee must review and act upon all NTRR minutes regardless whether the NTRR is established at the medical center or at the affiliate university.

(12) VA Handbook 1200.5, **9.c. Record Keeping.**

(a) Each IRB that uses an expedited review process must adopt a method for keeping all members advised of research proposals that have been approved under this process. The minutes and/or the protocol file must reflect the expedited review eligibility category that the research meets.

18. Reporting

a) See each specific grant contract for reporting requirements.

b) Federal regulations at

(1) 45 CFR 46 Subparts B - D

(2) 21 CFR 50 Subpart D

(3) 38 CFR 16

(4) Veterans Health Administration Handbook 1200.5

(5) May 2003 OHRP Guidance on the Involvement of Prisoners in Research

(6) May 2005 OHRP Guidance on the HHS 45 CFR 46.407 Review Process for Children Involved as Subjects in Research.

(7) Under 45 CFR 46 46.103(b) (3) reporting Changes in IRB membership to the department or agency head and / or Office for Human Research Protections

(8) Under 45 CFR 46 46.103(b) (4) and 21 CFR 56.108(a)(1) reporting its findings and actions concerning initial and continuing review to the investigator and the institution;

(9) Under 45 CFR 46 46.103(b) (5) prompt reporting to the IRB, appropriate institutional officials, and the department or agency head of (i) any unanticipated problems involving risks to subjects or others or any serious or continuing noncompliance with this policy or the requirements or determinations of the IRB; and (ii) any suspension or termination of IRB approval.

(10) Under 45 CFR 46 46.113 an IRB shall have the authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects. Any suspension or termination of approval shall include a statement of the reasons for the IRB's action and shall be reported promptly to the investigator, appropriate institutional officials, and the department or agency head.

(11) Under 21 CFR 56.108(b)(1) prompt reporting to the IRB, appropriate institutional officials, and the Food and Drug Administration of Any unanticipated problems involving risks to human subjects or others; any instance of serious or continuing noncompliance with these regulations or the requirements or determinations of the IRB; or any suspension or termination of IRB approval. (Note: FDA guidance interprets 108(b)(1) to require investigators to report these "unanticipated problems" to the IRB and sponsors to report serious unexpected events, including analyses of such events, to investigators and to FDA. Therefore, UTHSCSA policy shall include written procedures to confirm these activities occurred to comply with21 CFR 56.108(b)(1). Serious or continuing noncompliance and suspension or termination are determinations of the IRB and will be reported by the IRB to appropriate institutional officials, and the FDA as per this regulation.)

(12) Under 21 CFR 56.113, an IRB shall have the authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects. Any suspension or termination of approval shall include a statement of the reasons for the IRB`s action and shall be reported promptly to the investigator, appropriate institutional officials, and the Food and Drug Administration

(13) IRBs are required to function under written procedures. One of these procedural requirements [21 CFR 56.108(a)(3)] requires ensuring "prompt reporting to the IRB of changes in a research activity." The completion of the study is a change in activity and should be reported to the IRB. Although subjects will no longer be "at risk" under the study, a final report/notice to the IRB allows it to close its files as well as providing information that may be used by the IRB in the evaluation and approval of related studies. Therefore the UTHSCSA IRB will report its findings and actions concerning Final reports (which constitute changes in research activity under the FDA) to the investigator and the institution;

19. Adverse Event reporting (Adverse Events, Unanticipated problems, Unanticipated Adverse Drug Experiences, Unanticipated Adverse Device Effects)

a) For all non-exempt human studies,

(1) OHRP’s published guidance for use by Human Subject Protection Programs U.S. Department of Health and Human Services: Office for Human Research Protections. (January 15, 2007)

(2) Guidance for Clinical Investigators, Sponsors, and IRBs Adverse Event Reporting — Improving Human Subject Protection (Draft Guidance) U.S. Department of Health and Human Services: Food and Drug Administration April 2007,

(3) For drug studies,

(4) For device studies,

(a) investigators are required to submit a report of a UADE to the sponsor and the reviewing IRB as soon as possible, but in no event later than 10 working days after the investigator first learns of the event (§ 812.150(a)(1)).

(b) Sponsors must immediately conduct an evaluation of a UADE, and must report the results of the evaluation to FDA, all reviewing IRBs, and participating investigators within 10 working days after the sponsor first receives notice of the effect (§§ 812.46(b), 812.150(b)(1)).

20. Noncompliance

a) 21 CFR 56.123

b) 45 CFR 46.112

21. FDA regulated research

a) For all FDA Regulated research

(1) 21 CFR 50 and 56

b) For Emergency use - In addition to III.B.21.a) above:

(1) 21 CFR 56.102(d)

(2) 21 CFR 56.104(c)

(3) 21 CFR 50.23

(4) 21 CFR 312.36

(5) 21 CFR 812.

(6) FDA Information Sheet, Drugs and Devices 1998 (http://www.fda.gov/oc/ohrt/IRBs/drugsbiologics.html#emergency)

(7) FDA Information Sheet, Medical Devices 1998 (http://www.fda.gov/OC/OHRT/IRBS/devices.html#emergency)

(8) May 15, 1991, OPRR statement

c) Drugs - In addition to III.B.21.a) above:

(1) See 21 CFR 312

(2) Texas Food, Drug, and Cosmetic Act, Health and Safety Code, Title 25, Part 1, Chapter 229, Subchapter AA, Rule §229.543 Definitions

(a) an article or substance recognized in the official United States Pharmacopoeia, the official Homeopathic Pharmacopoeia of the United States, and the official National Formulary, or any supplement of them;

(b) an article or substance designed or intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals;

(c) an article or substance, other than food, intended to affect the structure or any function of the body of man or other animals; or

(d) an article or substance intended for use as a component of any article or substance specified in this definition..

d) Devices - In addition to III.B.21.a) above:

(1) See 21 CFR 812

(2) See 21 CFR 812.66 concerning significant risk device determinations.

(3) See 21 CFR 812.2(b)

(4) Texas Food, Drug, and Cosmetic Act, Health and Safety Code, Title 25, Part 1, Chapter 229, Subchapter AA, Rule §229.543 Definitions

(a) Device--An instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component; part, or accessory; that is:

(i) recognized in the official United States Pharmacopoeia National Formulary or any supplement to it;

(ii) intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease in man or other animals; or

(iii) intended to affect the structure or any function of the body of man or other animals and that does not achieve any of its principal intended purposes through chemical action within or on the body of man or other animals and is not dependent on metabolization for the achievement of any of its principal intended purposes.

(5) Exemptions

(a) See exemptions at 21 CFR 812.2(C)

(b) For clarification concerning devices previously cleared by the FDA, they are considered exempt from the requirement for prior submission to the FDA for an IDE before a clinical investigation when they are devices:

(i) with an approved PMA(812. (c)(4));

(ii) which have been cleared via a Premarket Notification 510(k)(812.2(c)(2));

(iii) which have been considered exempt under 510(k) (812.2(c)(2) referencing 807.85 which includes pre-1976).

(iv) considered to be a Pre-Amendments device.

(6) Reports to the IRB from the investigator and the sponsor

(a) 21 CFR 812.150.

22. Suspension or Termination

a) 21 CFR 56.113

b) 45 CFR 46.113

c) 38 CFR 16.113

23. HIPAA (See also Privacy and Confidentiality at III.B.9 above)

a) 45 CFR 164.512

b) 45 CFR 164.532

c) 45 CFR 164.530

d) 45 CFR 164.508

e) 45 CFR 164.514

f) NIH's Research Repositories, Databases, and the HIPAA Privacy Rule

g) NIH's Privacy Boards and the HIPAA Privacy Rule

C. When the proposed or revised existing NTRR Policy and Procedure is turned in to the NTRR Manager at the Draft Deadline by the NTRR Policy Subcommittee

1. The NTRR Manager or NTRR PI

a) Reviews and edits the policy

b) Returns the policy for further research/modification or;

c) Routes the policy to the NTI Staff to route as necessary through the NTRR Executive Committee and subsequently the full NTRR Steering Committee.

2. NTI Staff

a) Copy the draft policy and route as necessary to the applicable entities, appropriate NTI officials or NTRR committee or subcommittees.

D. When the proposed or existing NTRR Policy and Procedure is turned in to the NTRR Manager at the Final Deadline.

1. The NTRR Manager or NTRR PI

a) Reviews and edits the policy

b) Returns the policy for further research/modification or;

c) Routes the policy to the NTI Staff to route as necessary.

2. NTI Staff

a) Copy the Final policy and route as necessary to the applicable entities, appropriate NTI officials or NTRR committee or subcommittees.

b) The Final Draft of the Policy and Procedure is activated and posted to the NTRR website with the paper and electronic copies maintained in accordance with the Record Keeping Policy and Procedure.

IV. References

A. Definitions (see Glossary)

National Trauma Research Repository (NTRR)

Data Storage and Sharing Policy

Contents

Overview

The National Trauma Research Repository (NTRR) is a central repository and resource for sharing data that was developed by the Department of Defense (DoD) and the National Trauma Institute (NTI) to promote collaboration, accelerate research, and advance knowledge on the characterization, prevention, diagnosis and treatment of trauma. NTRR provides a common platform and standardized format for data collection, retrieval and archiving, while allowing for flexibility in data entry and analysis. Additional information and detailed implementation guidance related to the NTRR can be found at the NTRR website.

Expectations Defined in the Data Sharing Policy for Investigators

The detailed expectations are enumerated in the individual sections of this data sharing policy, and summarized as follows:

Contributing Investigators submitting data to NTRR are expected to:

• Submit a Data Submission Form, providing assurance that all data are submitted in accordance with applicable laws and regulations, and that the identities of research participants will not be disclosed to the NTRR; and
• Upload ALL data to NTRR on a quarterly basis.

Recipient Investigators requesting and receiving NTRR data are expected to:

• Submit a Data Access Request;
• Protect data confidentiality;
• Ensure that adequate data security measures are in place;
• Notify the NTRR Executive Committee of policy violations;
• Submit annual progress reports detailing significant research findings; and
• Include acknowledgements of the NTRR in all publications and presentations.

Applicability

This Data Sharing Policy applies to:
• DoD and other federal (e.g., Department of Health and Human Services (DHHS)) extramural and intramural research projects that include trauma clinical studies, defined as:

- Patient-oriented research. Research conducted with human subjects (or on material of human origin such as tissues, specimens, and cognitive phenomena) for which an investigator (or colleague) directly interacts with human subjects. Excluded from this definition are *in vitro* studies that utilize human tissues that cannot be linked to a living individual. It includes:
    - mechanisms of human disease;
    - therapeutic interventions;
    - clinical trials;
    - development of new technologies;
- Epidemiological and behavioral studies;
- Outcomes research and health services research.

• Research studies supported by other agencies and groups who would like to deposit data into the NTRR.

Oversight and Governance of NTRR

The DoD and the NTI have developed a governance structure for NTRR to provide oversight. The NTRR Policy Subcommittee oversees the NTRR Data Sharing Policy and its implementation. In carrying out this responsibility, the chair participates on a NTRR Executive and Steering Committees, which is responsible for the on-going management and stewardship of NTRR Data Sharing Policy and Procedures. Reporting to the NTRR Executive and Steering Committees are several groups and teams charged with the implementation, communication, and development of specific procedures related to the conduct, submission, and data release practices for NTRR. Of these groups, the NTRR Policy Subcommittee is responsible for overseeing NTRR Data Sharing Policy and together with the NTRR Regulatory Subcommittee, is responsible for overseeing Data Access to promote consistent and robust participant protections in NTRR.

NTRR Data Sharing Policy addresses (1) data sharing procedures, (2) data access principles, and (3) issues regarding the protection of research participants during the submission of, storage of, and access to data within the NTRR. The goal of the policy is to advance science for the benefit of the public through the creation of a centralized Federal data repository for trauma research information. The principles contained in this policy were developed by the NTRR Policy Subcommittee and are consistent with existing NTI and DoD polices on data sharing. The DoD and the NTI recognize that scientific, ethical, and societal issues relevant to this policy are evolving, and have established a Policy Subcommittee to oversee implementation and data use practices. The agencies will revisit and revise the policy and related practices as appropriate.

Data Management

Protecting Research Participants

The potential for public benefit to be achieved through sharing trauma research data is significant. However, the broad data distribution goals of NTRR highlight the importance of protecting the privacy of the research participants and the confidentiality of their data. NTRR Data Sharing Policy includes steps to protect the interests and privacy concerns of individuals, families, and identifiable groups who participate in genetic and other research. The informed consent process is a critical step and subject consent forms in prospective studies should include language similar to the following:

> "All links with your identity will be removed from the data before they are shared. Only de-identified data which do not include anything that might directly identify you will be shared with National Trauma Research Repository (NTRR) users and the general scientific community for research purposes."

For retrospective studies conducted before the development of NTRR, the agencies anticipate considerable variation in the extent to which data sharing and future research have been addressed within the informed consent documents. The submitting institution will determine whether a study is appropriate for submission to NTRR (including an Institutional Review Board (IRB) and/or Privacy Board review of specific study elements, such as participant consent). Some studies may require additional consent of the research participants. To ensure the security of the data held in the NTRR, NTI will employ multiple tiers of data security based on the content and level of risk associated with the data. NTRR will establish and maintain operating policies and procedures to address issues including, but not limited to, the privacy and confidentiality of research participants, the interests of individuals and groups, data access

procedures, and data security mechanisms. These will be reviewed periodically by the NTRR oversight bodies as appropriate.

HIPAA and Validation of Data Made Available by NTRR

NTI is not a HIPAA covered entity (there is no electronic medical billing related to intramural/Clinical Center study participants). NTRR, being part of NTI, is also not a HIPAA covered entity. However, the HIPAA De-identified Dataset definition will be used as the basis for this certification.

1. Specifically, NTRR contributors, as covered entities, must ensure that the following direct identifiers of the research subject or of relatives, employers, or household members associated with the research subject are removed prior to upload as per the NTRR Data Sharing Policy:

    (A) Names;

    (B) All geographic subdivisions smaller than a State, including street address, city, county, precinct, zip code, and their equivalent geocodes, except for the initial three digits of a zip code if, according to the current publicly available data from the Bureau of the Census: (1) The geographic unit formed by combining all zip codes with the same three initial digits contains more than 20,000 people; and (2) The initial three digits of a zip code for all such geographic units containing 20,000 or fewer people is changed to 000.

    (C) All elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death; and all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older;

    (D) Telephone numbers;

    (E) Fax numbers;

    (F) Electronic mail addresses;

    (G) Social security numbers;

    (H) Medical record numbers;

    (I) Health plan beneficiary numbers;

    (J) Account numbers;

    (K) Certificate/license numbers;

    (L) Vehicle identifiers and serial numbers, including license plate numbers;

    (M) Device identifiers and serial numbers;

(N) Web Universal Resource Locators (URLs);

(O) Internet Protocol (IP) address numbers;

(P) Biometric identifiers, including finger and voice prints;

(Q) Full face photographic images and any comparable images; and

(R) Any other unique identifying number, characteristic, or code, except as permitted by paragraph (T) of this section; and

2. The contributing investigator's covered entity must also not have actual knowledge that the information could be used alone or in combination with other information to identify an individual who is a subject of the information
3. A contributing investigator's covered entity may assign a code or other means of record identification to allow information de-identified under this section to be re-identified by the contributing investigator's covered entity only, provided that: (1) Derivation. The code or other means of record identification is not derived from or related to information about the individual and is not otherwise capable of being translated so as to identify the individual; and (2) Security. The covered entity does not use or disclose the code or other means of record identification for any other purpose, and does not disclose the mechanism for re-identification.

Any potential discrepancies to this privacy rule (e.g., genomics data or images that could be transformed) will be documented and approved/denied by the NTRR Data Access and Quality Committee (DAQC).

The Privacy Rule: What Information is Protected?

Protected Health Information. The Privacy Rule protects all *"individually identifiable health information"* held or transmitted by a covered entity or its business associate, in any form or media, whether electronic, paper, or oral. The Privacy Rule calls this information "protected health information (PHI)." "Individually identifiable health information" is information, including demographic data, that relates to:

- the individual's past, present or future physical or mental health or condition,
- the provision of health care to the individual, or
- the past, present, or future payment for the provision of health care to the individual,

and that identifies the individual or for which there is a reasonable basis to believe it can be used to identify the individual. Individually identifiable health information includes many common identifiers (e.g., name, address, birth date, Social Security Number).

The Privacy Rule excludes from protected health information employment records that a covered entity maintains in its capacity as an employer and education and certain other records subject to, or defined in, the Family Educational Rights and Privacy Act, 20 U.S.C. §1232g.

De-Identified Health Information. There are no restrictions on the use or disclosure of de-identified health information. De-identified health information neither identifies nor provides a

reasonable basis to identify an individual. There are two ways to de-identify information; either: (1) a formal determination by a qualified statistician; or (2) the method described above, removal of specified identifiers of the individual and of the individual's relatives, household members, and employers is required, and is adequate only if the covered entity has no actual knowledge that the remaining information could be used to identify the individual.
http://www.hhs.gov/ocr/privacy/hipaa/understanding/summary/index.html

To Whom Does the Privacy Rule Apply and Whom Will It Affect?

Key Points:

- The Privacy Rule applies only to covered entities. Many organizations that use, collect, access, and disclose individually identifiable health information will not be covered entities, and thus, will not have to comply with the Privacy Rule.
- The Privacy Rule does not apply to research; it applies to covered entities, which researchers may or may not be or be an agent or employee of. The Rule may affect researchers because it may affect their access to information, but it does not regulate them or research, per se.
- To gain access for research purposes to PHI created or maintained by covered entities, the researcher may have to provide supporting documentation on which the covered entity may rely in meeting the requirements, conditions, and limitations of the Privacy Rule.
- To gain access for research purposes to de-identified data created or maintained by covered entities or non-covered entities does not require any specific requirement, condition or limitation per the Privacy Rule.

In conclusion, NTI is not a HIPAA covered entity (there is no electronic medical billing related to intramural/Clinical Center study participants). NTRR, being part of NTI, is also not a HIPAA covered entity.

http://privacyruleandresearch.NIH.gov/pr_06.asp

Non-Research Use of Data

As agencies of the Federal Government, the DoD and NTI are required to release Government records in response to a request under the Freedom of Information Act (FOIA), unless they are exempt from release under one of the FOIA exemptions. Although the NTRR-held data will be de-identified, and neither the DoD nor NTI will hold direct identifiers to individuals within the NTRR, the agencies recognize the personal and potentially sensitive nature of the genotype-phenotype data. The DoD and the NTI believe that release of un-redacted NTRR datasets in response to a FOIA request would constitute an unreasonable invasion of personal privacy under FOIA Exemption 6, 5 U.S.C. § 552 (b)(6). Therefore, among the safeguards that the agencies foresee using to preserve the privacy of research participants and confidentiality of genetic data are the redaction of individual-level genotype, phenotype, and other clinical data from disclosures made in response to FOIA requests and the denial of requests for un-redacted datasets.

In addition, the DoD and NTI acknowledge that legitimate requests for access to data made by law enforcement offices to NTRR may be fulfilled. Neither the DoD nor NTI will possess direct identifiers within the NTRR Informatics System, nor will the agencies have access to the link between any data code and the identifiable information that may reside with the contributing primary investigators or contributing institutions for particular studies. The release of identifiable information may be protected from compelled disclosure by the primary investigator's institution if a Certificate of Confidentiality is or was obtained for the original study. The NTI and the DoD explicitly encourage investigators to consider the potential appropriateness of obtaining a Certificate of Confidentiality (http://grants.nih.gov/grants/policy/coc/) as an added measure of protection against future compelled disclosure of identities for studies planning to collect genome-wide association data. These confidentiality provisions may not apply to military subjects' chains of command.

Data Submission

DoD-supported and other federal (e.g., DHHS) human trauma research studies—including both intramural and extramural studies—will be required to have a data management plan which may be satisfied by depositing de-identified data into the NTRR. Research studies funded by other agencies and groups may also deposit de-identified data into the NTRR, pending review by the NTRR Steering Committee in collaboration with the external funding source on a case-by-case basis, deferring to pre-existing policies, regulations, and constraints. Potential contributing investigators, applying for funding from participating agencies, will be asked to include a data sharing plan consistent with NTRR policy as part of their application and are expected to use the Core NTRR Common Data Elements (CDEs) at a minimum. NTI's NTRR Operations teams will work with researchers to map their study variables to specific certified CDEs or new uncertified CDEs (UCDEs). In addition, NTI will consult with researchers to ensure the formats of the CDEs collected are compatible with the NTRR. In addition to CDE variables, NTRR will accept raw data from imaging, biomarker, or physiologic studies, additional supporting documentation as follows:

- the study protocols;
- manual of operations;
- variables measured;
- case report forms; and
- other relevant documents.

All data and information will be submitted to a high security network within NTI through a secure transmission process, including the supporting documentation:

Data submitted to the NTRR will be certified as de-identified by the Contributing Investigator such that the identities of data subjects cannot be readily ascertained or otherwise associated with the data by the NTRR staff or secondary data users.

Contributing Investigators submitting datasets to NTRR are expected to certify that an appropriate IRB has considered such risks and that the data have been de-identified in accordance with DoD and other federal regulations (e.g., HIPAA) before the data are submitted. In addition, in the event that requests raise questions or concerns related to privacy and confidentiality, risks to populations or groups, or other relevant topics, the NTRR Steering Committee will consult with other experts as appropriate.

Submissions of data to NTRR shall be accompanied by a certification signed by the Principal

Investigator to assure that:
• The data submission is consistent with all applicable laws and regulations, as well as institutional policies;
• The appropriate research uses of the data and the uses that are explicitly excluded by the informed consent documents are delineated;
• The identities of research participants will not be disclosed to the NTRR/NTI; and
• An IRB of the contributing institution and/or Privacy Board, as applicable, reviewed and verified that:
  o The submission of data to the NTRR and subsequent sharing for research purposes to recipient investigators are consistent with the informed consent of study participants from whom the data were obtained;
  o The investigator's plan for de-identifying datasets is consistent with the standards outlined above;
  o The risks to individuals, their families, and groups or populations associated with data submitted to the NTRR have been considered; and
  o The genotype and/or phenotype data to be submitted were collected in a manner consistent with DoD and NIH regulations and policies.

While the agencies expect data sharing through this policy, circumstances beyond the control of investigators may preclude submission of trauma research data to the NTRR. Applications submitted to these agencies for support of trauma research in which the above expectations for data submission cannot be met will be considered for funding on a case-by-case basis by the relevant agency. Potential Contributing Investigators are encouraged to submit a short list of planned papers on primary and secondary study objectives to their science officers when negotiating data sharing plans/requirements.

Data Submission Schedule
Data include all research and clinical assessments and information obtained via interviews, direct observations, laboratory tasks and procedures, records reviews, genetic and genomic data, neuroimaging data, neuropsychological assessments, data from physical examinations, etc. In addition, supporting documentation that is needed to enable an investigator unfamiliar with the dataset to understand and use the data is also required. For example, supporting documentation may include non-copyrighted data collection forms, study procedures and protocols, data dictionary rationale, exclusion criteria, website references, a listing of major study publications, and the definition of a genomic analysis protocols. The following are not included as data: laboratory notebooks, preliminary analyses, drafts of scientific papers, plans for future research, peer review reports, communications with colleagues, or physical objects, such as gels or laboratory specimens. All data* will be submitted to NTRR on a quarterly basis according to the following schedule:

Data collection period	Quarterly upload due
January 1 – March 31	June 30
April 1 – June 30	September 30
July 1 – September 30	December 31
October 1 – December 31	March 31

* Clinical trials are exempted from this schedule; all data from clinical trials must be submitted within a year following the end of the performance period of the award.

NTRR Data Sharing Schedule

Six months after submission of the data, the ***Core*** (required) and ***Basic*** (certified and uncertified, recommended) trauma research common data elements (***CDEs and UCDEs***) that are used in the study (except Experimental Data) will be made available to all qualified and approved researchers (Recipient Investigators) as determined by the NTRR Steering Committee. Other data fields can also be made available at the submitting principal investigator's (Contributing Investigator's) discretion. Outcomes data and other data elements needed by the principal investigator to test his/her hypotheses or research questions, referred to as ***Experimental Data***, will be made available in a staged manner. Six months after the award period ends, ***Experimental Data*** will be open to other researchers who have submitted data to NTRR (Contributing/Recipient Investigators). Twelve months after the award period ends, ***Experimental Data*** will be open to all qualified and approved researchers (Recipient Investigators)**.**

Summary of the NTRR Data Sharing Schedule

Core and Basic CDEs	Data are uploaded quarterly after subject enrollment begins and data are available six months after submission to all approved NTRR Data Recipients. Specific CDEs can be exempted pending approval by the NTRR Steering Committee if they are needed to test the primary study hypothesis or research question.
Experimental Data	All approved NTRR Data Recipients gain access either: a) Six months after the award period ends if they are a NTRR Submitter; or b) Twelve months after the award period ends for those who are not NTRR Submitters. Access can also be granted earlier if agreed to by the Submitters of ongoing study(s) or in rare cases when the NTRR Steering Committee over rules the Submitters' denial on the grounds that the request does not compromise completion of the ongoing study.

Contributing and Recipient Investigators are also strongly encouraged to collaborate and share data throughout a study's period of performance to accelerate research and advance knowledge of trauma. To facilitate collaboration, data access request forms may be submitted by Recipient Investigators before the end of the performance period to the NTRR Steering Committee for initial review and then forwarded on to the Contributing Investigators. The Contributing Investigators may choose to collaborate and/or to provide access to all or some of their ***Experimental Data***, in which case the data will be made available to the data recipients (Recipient Investigators). Alternatively, the Contributing Investigators may choose to deny early access, in which case the request will be reviewed by the NTRR Steering Committee in consultation with the Contributing Investigators. In this case, approvals for early access will only be granted by the NTRR Steering Committee if it is clear that the data request does not negatively impact the completion of the original study. For example, prospective data collection projects that are powered to answer specific questions would be jeopardized by premature analysis of these same questions. However, if important research can be accomplished without jeopardizing the study, the value of the NTRR data will be greatly enhanced by data sharing that advances the science of trauma.

NTRR Data Access

NTRR will provide descriptive summary information of Contributing Investigator data for general public use. Access to data for research purposes will be provided through the NTRR Steering Committee. Membership of the NTRR Steering Committee will include Federal staff with expertise in areas such as the relevant particular scientific disciplines, research participant protection, and privacy. The NTRR Steering Committee will operate according to common principles and follow similar procedures to ensure the consistency and transparency of the NTRR data access process. The NTRR Steering Committee will review the applications of investigators requesting data and make a determination based on their affiliation with a research institution, and on the basis of the reason for the request. It is anticipated that most requests will be appropriate and can be approved rapidly, and that only a few will require clarification. In the event that requests raise concerns related to privacy and confidentiality, risks to populations or groups, or other concerns, the NTRR Steering Committee will consult with other experts as appropriate. A request to appeal the decision is allowed and will be reviewed by the NTRR Policy Committee.

Investigators and institutions seeking data from the NTRR will be expected to meet data security measures (such as physical security, information technology security, and user training) and will be asked to submit a Data Access Request that is signed by the Recipient Investigator. Data Access Requests should include a brief description of the proposed research use of the requested NTRR data. Investigators will agree, among other things, to:

- Use the data only for the approved research; if the Recipient Investigator wants to use the data to investigate additional research questions, a second data access request form must be submitted.
- Protect data confidentiality;
- Follow appropriate data security protections;
- Follow all applicable laws, regulations and local institutional policies and procedures for handling NTRR data;
- Not attempt to identify individual participants from whom data within a dataset were obtained;
- Not sell any of the data elements from datasets obtained from the NTRR;
- Not share with individuals other than those listed in the request any of the data elements from datasets obtained from the NTRR;
- Agree to the list of approved research uses within the NTRR along with his/her name and organizational affiliation;
- Provide IRB numbers and expiration dates;
- Agree to report, in real time, violations of the NTRR Data Sharing Policy to the NTRR Executive Committee;
- Adhere to the NTRR Data Sharing Policy below with regard to publication; and
- Provide annual progress reports on research using NTRR data.

Data Quality

The DoD and NTI are implementing a two-tiered data control procedure for information and images submitted to the NTRR to ensure that the information submitted has undergone reviews for accuracy, completeness, and availability. The first level of quality control is performed by the researcher who is expected to certify the accuracy of the information prior to submission. The second level of quality control occurs when data and/or images are submitted to the NTRR for broad research access. NTRR will provide a period of three months to allow the Submitter and

the agencies to undertake activities to review the completeness of the submission. Such efforts include verifying that the information received by NTRR will be complete (i.e., not missing records intended for submission), contains no identifying information, and displays correctly. During this timeframe, access to data and images for research is temporarily suspended to help ensure that NTRR makes available only carefully reviewed information. Should the agencies determine that additional time is necessary to ensure the quality of the submitted information (e.g., time necessary to remedy concerns), the agencies may opt to extend the quality control period as necessary in the interest of science. After quality control measures are satisfied, the submitted information will be certified as accurate by the submitting researcher.

Publication

The DoD and NTI strongly encourage collaboration, but at a minimum all investigators who access NTRR data are expected to acknowledge the funding organization(s) that supported their work, the Contributing Investigator(s) who conducted the original study, and the NTRR in all resulting presentations, disclosures, or publications of the analyses. Data Recipients should submit manuscripts to the NTRR Steering Committee for administrative review at least four weeks prior to submission for publication. This review is not a scientific review, but an administrative review to ensure that the terms of the user agreement have been met, the description of NTRR procedures are accurately identified, and NTRR and the original researchers are appropriately acknowledged. These administrative reviews will take no longer than two weeks.

National Trauma Research Repository (NTRR)

Data Access Request (DAR) &
Data Use Certification (DUC)

Contents

NTRR Data Access Request

The NTRR Steering Committee approves access to data and/or images from the National Trauma Research Repository (NTRR) for research purposes only. The NTRR Steering Committee will review the Data Access Request (DAR) and the Data Use Certification (DUC) of each applicant requesting data and provide access based on the expectations outlined in the NTRR policy. These expectations include the protection of data privacy, confidentiality, and security. In the event that requests raise concerns related to privacy and confidentiality, risks to populations or groups, or other concerns, the NTRR Steering Committee will consult with other experts as appropriate.

Recipient Investigators seeking access to data or images from NTRR are expected to submit their DAR and DUC, signed by the Principal Investigator. Completing this DAR is a necessary step to access data or images from NTRR.

Steps to Request Query Access to the NTRR

1. Read the NTRR Data Use Certification (DUC) below.
2. Provide a scanned copy of the signed DUC Recipient Investigator Information and Certifications page when requesting an account to NTRR (with Query and Study privileges) at the NTRR website.
3. Access Request Review: The NTRR Steering Committee will review requests to access the NTRR. Such reviews are generally completed within 10 business days.
4. The NTRR Steering Committee will notify NTI staff if the access request has been approved, and an account will then be provided. Users will receive an automated notification of their account update with any modified user name, passwords, or instructions for accessing the NTRR.
5. Optional: NTRR System Training (if request approved): Contact NTRR via email at research@nationaltraumainstitute.org to discuss specific training needs the user may have and schedule the training.

Data Use Certification (DUC) for the National Trauma Research Repository (NTRR)

Introduction

The Department of Defense (DOD) and the National Trauma Institute have developed a repository to store the collection of data from traumatic research studies, regardless of the source of funding. The extensive information collected by these studies, and subsequently stored in the National Trauma Research Repository (NTRR), provides a rare and valuable scientific resource. Promoting optimal use on a national scale of this resource will require a large and concerted effort, which may exceed the research capacity of currently investigators. DOD and the NTI have responsibility to the public in general, and to the scientific community in particular, to encourage the use of these resources to achieve rapid scientific progress. In order to take full advantage of such resources and maximize their research value, it is important that data be made available, on appropriate terms and conditions, to the largest possible number of qualified investigators in a timely manner.

Data collected by the Contributing Investigator have been stripped of all direct identifiers, but the unique and intrinsically personal nature of DNA, derivative data of which are included in NTRR, combined with the recent increase in the accessibility of conducting genotype and other sequence analyses (in terms of technological capacity and cost), has altered the framework through which “identify-ability” can be defined. To protect and assure the confidentiality and privacy of all participants, the Recipient Investigator who is granted access to these data is expected to adhere to the specifications of this DUC. Failure to do so could result in denial of further access to data and subject the Recipient Investigator of any other applicable penalties and actions.

Contributing Investigators have made a substantial long-term contribution to NTRR by submitting data to the repository. DoD and NTI seek to encourage appropriate data use and collaborative relationships by Recipient Investigators with the Contributing Investigators and to ensure that the contribution of the Contributing Investigator is appropriately acknowledged.

Definitions

For purposes of this agreement:

“Data” refers to the information that has been collected and recorded from participants in trauma research studies, regardless of the source of funding. Data from study participants were collected through the periodic examinations and follow-up contacts, conducted pursuant to the Contributing Investigators’ Cooperative Agreements grants, other grants, contracts, and other trauma studies.

A “Contributing Investigator” is defined as a researcher who has submitted data to the NTRR, according to the policies laid out in the NTRR Submission Agreement. The Contributing Investigator may have had a past or current/active grant, contract, or consulting agreement with DoD or NTI, one of its contractors, or any other funding source.

The “Recipient Investigator” Principal Investigator is an individual who seeks access to data from NTRR. The Recipient and his/her Organization may be a researcher at a non-profit or for-profit organization or corporation with or without an approved assurance from the Department of Health and Human Services Office for Human Research Protections (OHRP) or the DoD. The Recipient requests access to study data at his/her sole risk and at no expense to the study, DoD, and NTI.

Terms and Conditions

I request approval to access data and/or images from the National Trauma Research Repository (NTRR) for research purposes. I agree to the following terms:

1. Research Project. These data will be used by Recipient Principal Investigator solely in connection with the “Project Summary/Abstract” “. If the Project does involve Recipient Investigator(s), their names and the work they will perform are also included in the Recipient Information and Certifications section.

This DUC covers only the Research Project contemplated in the Project Summary/Abstract section. Recipient agrees that data will not be used in any research that is not disclosed and approved as part of the Research Project. Recipient will submit a completed DUC (this document) for each research project for which data are requested. This applies to all versions of NTRR data. Recipient will submit a completed DUC (this document) for each research project for which data are requested. This applies to all versions of NTRR data.

2. Non-transferability of Agreement. This DUC is not transferable. Recipient Investigator agrees that any substantive change Recipient Investigator makes to the Research Project requires execution and approval of a new DUC, in which the new Research Project is designated. If the Recipient Investigator appoints another Principal Investigator to complete the Research Project, a new DUC in which the new Recipient Investigator is designated is necessary. If the Recipient Investigator changes institutions and wishes to retain access to NTRR data, a new DUC must be executed and approved.

3. Non-Identification of Subjects. Recipient Investigator agrees that data will not be used, either alone or in conjunction with any other information, in any effort whatsoever to establish the individual identities of any of the subjects from whom data were obtained. Recipient Investigator agrees to notify NTRR as soon as possible if, upon use of NTRR data, the Recipient Investigator discovers identifying information in those data.

4. Data Disclaimers. Recipient agrees that DoD and NTI do not and cannot warrant the results that may be obtained by using any data included therein. DoD and NTI disclaim all warranties as to the accuracy of the data in NTRR or the performance or fitness of the data for any particular purpose.

5. Notification of NTRR of Publication. Prompt publication or other public disclosure of the results of the Research Project is required. Recipient Investigator agrees to notify NTRR via email as to when and where a publication (or other public disclosure) of a report from the Research Project will appear. Notification of such publications can occur by sending to NTRR research@nationaltraumainstitute.org an updated biographical sketch or CV of the publishing author.

6. Data Access for Research. Data from active and completed studies are eligible for restricted "Controlled Access" by qualified Recipient Investigator pursuant to the terms set forth in this agreement. Recipient Investigator of Controlled Access data acknowledge that other researchers have access to the data and that downloading, utilization, and duplication of research are distinct possibilities.

7. No Distribution of Data. Recipient Investigator agrees to retain control over data, and further agrees not to transfer data, with or without charge, to any other entity or any individual, except for collaborators with approved DUCs. Recipient Investigator agrees not to sell the data in any form to any entity or individual or to distribute the data to anyone other than his/her research staff and collaborators with an approved DUC, who will also agree to the terms within this DUC.

8. Acknowledgments. Recipient Investigator agrees to acknowledge the contribution of the NTRR bioinformatics platform, the relevant NTRR dataset identifier(s) (a serial number), and the Contributing Investigator(s) in any and all oral and written presentations, disclosures, and publications resulting from any and all analyses of data using the NTRR tools, whether or not Recipient Investigator is collaborating with Contributor Investigator(s). The manuscript should include the following acknowledgement or other similar language:

> Data and/or research tools used in the preparation of this manuscript were obtained and analyzed from the controlled access datasets distributed from the DoD and NTI-supported National Trauma Research Repository (NTRR). NTRR is a collaborative biomedical repository created by the Department of Defense and the National Trauma Institute (NTI) to provide a national resource to support and accelerate research on trauma.

If the Research Project involves collaboration with Contributing Investigators or NTRR staff then Recipient Investigator will acknowledge Contributor Investigator or NTRR staff as co-authors, if appropriate, on any publication. In addition, Recipient Investigator agrees to include a reference to NTRR datasets analyzed and to cite NTRR and the federal funding sources in abstracts as space allows.

9. Non-Endorsement; Liability. Recipient Investigator agrees not to claim, infer, or imply endorsement by the United States Government, the Department of Defense, the Department of Health & Human Services, or the National Trauma Institute, the entity, or personnel conducting the Research Project or any resulting commercial product(s). The United States Government assumes no liability except to the extent provided under the Federal Tort Claims Act (28 U.S.C. § 2671-2680).

10. Recipient Investigator Compliance with Institutional Requirements. Recipient Investigator acknowledges that access to NTRR data, if provided, is for research that must be authorized by the Recipient Investigator's Institution, which may or may not require operation under an Office of Human Research Protections (OHRP)-approved Assurance as determined by the institution. Furthermore, Recipient Investigator agrees to comply with all applicable DoD and DHHS/FDA rules for the protection of human subjects, and other federal and state laws for the use of these data. Recipient Investigator agrees to report promptly to NTRR any proposed change in the research project and any unanticipated problems involving risks to subjects or others. This DUC is made in addition to, and does not supersede, any of Recipient Investigator' s institutional policies or any local, State, and/or Federal laws and regulations that provide additional protections for human subjects.

11. Recipient Investigator's Permission to Post Information Publicly. Recipient Investigator agrees to permit DoD and NTI to summarize on the NTI Web site the Recipient Investigator's research use of NTRR along with the Recipient Investigator's name and organizational/institutional affiliation.

12. Privacy Act Notification. In order to access the NTRR, the Recipient Investigator agrees to provide the information requested below.

The Recipient Investigator agrees that information collected from the Recipient, as part of the Data Access Request, may be made public in part or in whole for tracking and reporting purposes. This Privacy Act Notification is provided pursuant to Public Law 93-579, Privacy Act of 1974, 5 U.S.C. Section 552a. Authority for the collection of the information requested below from the Recipient Investigator comes from the

authorities regarding the establishment of NTI, its general authority to conduct and fund research and to provide training assistance, and its general authority to maintain records in connection with these and its other functions. These records will be maintained in accordance with the Privacy Act System of Record Notice 09-25-0156 (http://oma.od.nih.gov/ms/privacy/pa-files/0156.htm) covering "Records of Participants in Programs and Respondents in Surveys Used to Evaluate Programs of the Public Health Service, HHS/PHS/NIH/OD." The primary uses of this information are to document, track, and monitor and evaluate the use of the NTRR Informatics datasets, as well as to notify interested recipients of updates, corrections or other changes to the database.

The Federal Privacy Act protects the confidentiality of the Recipient's DoD and NTI records. DoD and The Federal Privacy Act protects the confidentiality of the Recipient's DoD and NTI records. DoD and NTI and any sites that are provided access to the datasets will have access to the data collected from the Recipient for the purposes described above. In addition, the Act allows the release of some information in the Recipient Investigator's records without his/her permission; for example, if it is required by members of Congress or other authorized individuals. The information requested is voluntary, but necessary for obtaining access to data.

13. Security. Recipient acknowledges the expectations set forth by the attached "NTRR Information Security Best Practices" for the use and security of data.

14. Annual Update. Recipient will provide to research@nationaltraumainstitute.org an annual summary of research accomplishments from using NTRR and an updated biographical sketch http://grants.nih.gov/grants/funding/2590/biosketchsample.pdf or CV. Future access to NTRR will be contingent upon receiving the annual update.

15. Amendments. Amendments to this DUC must be made in writing and signed by authorized representatives of all parties.

17. Termination. Either party may terminate this DUC without cause by providing 30 days written notice to the other party. Recipient Investigator agrees to immediately report violations of NTRR Policy to the NTRR Steering Committee. Additionally, DoD and NTI may terminate this agreement with 5 days written notice if the DoD and NTI determine, in their sole discretion, that the Recipient Investigator has committed a material breach of this DUC. DoD and NTI may, in their sole discretion, provide Recipient Investigator with 30 day-notice to remedy a breach before termination. Upon termination of the DUC, use of the data must be discontinued. Closed accounts may be reactivated upon submission of an updated Access Request and DUC.

18. One Year Term and Access Period. Accounts with active grants are valid for one year and will be renewed annually by the NTRR operations team. This access will terminate 180 days following project/grant end date. Accounts that remain inactive for 12 consecutive months may be closed at the discretion of DoD and NTI.

19. Accurate Representations. Recipient expressly certifies that the contents of any statements made or reflected in this document are truthful and accurate**.**

NTRR Information Security Best Practices

The purpose of these Security Best Practices, which are subject to applicable law, is to provide minimum security standards and best practices for individuals who use NTRR to submit, access, and analyze data. Keeping NTRR information secure through these best practices is important. Subject to applicable law, Recipient Investigators agree to immediately report breaches of data confidentiality to the NTRR Steering Committee at research@nationaltraumaresearchinstitute.org.

Best Practices

• Do not attempt to override technical or management controls to access data for which you have not been expressly authorized.

• Do not use your trusted position and access rights to exploit system controls or access data for any reason other than in the performance of the proposed research.
• Ensure that anyone directed to use the system has access to, and is aware of, NTRR Information Security Best Practices and all existing policies and procedures relevant to the use of NTRR, including but not limited to, the NTRR policy at the NTRR website.
• Follow the NTRR password policy which includes:
    • Choose passwords of at least seven characters including at least three of the following types of characters: capital letters, lower case letters, numeric characters and other special characters.
    • Change your passwords every six months.
• Protect your NTRR password from access by other individuals—for example, store it electronically in a secure location.
• Notify NTRR staff, as permitted by law, at research@nationaltraumaresearchinstitute.org, of security incidents, or any incidents of suspected fraud, waste or misuse of NTRR or when access to NTRR is no longer required.

Security Standards
• Protect the data, providing access solely to authorized researchers permitted access to such data by your institution or to others as required by law.
• When you download NTRR data, download the data to a secured computer or server with strong password protection.
• For the computers hosting NTRR data, ensure that they have the latest security patches and are running virus protection software.
• Make sure the data are not exposed to the Internet or posted to a website that may be discovered by Internet search engines such as Google or MSN. Internet search engines such as Google or MSN.
• If you leave your office, close out of data files or lock your computer. Consider the installation of a timed screen saver with password protection.
• Avoid storing data on a laptop or other portable medium. If storing data on such a device, encrypt the data. Most operating systems have the ability to natively run an encrypted file system or encrypt portions of the file system. (Windows = EFS or Pointsec and Mac OSX = File Vault)
• When finished using the data, destroy the data or otherwise dispose of it properly, as permitted by law.

3a NTRR Data Access Request DAR

National Trauma Research Repository (NTRR)

Data Submission Request

Contents

NTRR Data Submission Request

The NTRR Steering Committee approves submission of data and/or images to the NTRR. The NTRR Steering Committee will review the Data Submission Request and will decide whether to permit the submission based on the expectations outlined in the NTRR policy. In the event that submissions raise concerns related to privacy and confidentiality, risks to populations or groups, or other concerns, the NTRR Steering Committee will consult with other experts as appropriate. In unusual circumstances, when people are denied approval to submit data, appeals may be sent to the NTRR Policy Subcommittee.

Contributing Investigators may use this Data Submission Request to 1) only submit data to NTRR or 2) submit data to NTRR and for subsequent analysis with NTRR tools by the Contributing Investigator. Both types of requests are subject to approval by the NTRR Steering Committee. Completing this Data Submission Request is a necessary step to submit data to NTRR. Access to other data within NTRR for analysis purposes may be subject to the NTRR Data Access Request and procedures.

Steps to Request to Contribute Data and/or Images to NTRR

1. Contact NTI through research@nationaltraumainstitute.org to set up an introductory phone call to begin planning for data submission. The NTRR staff will discuss with Contributing Investigators a) data submission expectations; b) supporting materials submission expectations; c) data access preferences; d) technical specifications; and e) data accuracy as it relates to NTRR. Contacting NTI two months before the desired date of submission is recommended to provide ample time to resolve technical and other issues.
2. Review the capabilities of NTRR at the NTRR website.
3. If NTRR can accommodate the data per discussions with the NTRR staff, read the NTRR Data Submission Agreement (SA) and complete and sign the SA on the Contributor Information and Certifications form (below).
4. Request a NTRR portal account under the “Request an Account” tab. When creating an account, request access to submit data to NTRR (Study Privilege).
5. When requesting to create a Study in NTRR, submit the Data Submission Agreement (SA).
6. Data submission review: The NTRR Steering Committee will review requests to submit data to the NTRR System. Such reviews are generally completed within 10 business days.
7. The NTRR Steering Committee will notify the Contributing Investigator if the submission request has been approved and an account will then be provided.

Once a contributor has permissions to submit data to NTRR, he or she should follow the steps for data submission as defined at the NTRR website.

Data Submission Agreement for the National Trauma Research Repository (NTRR)

I request approval to submit data and/or images to the National Trauma Research Repository (NTRR) for the purpose of sharing data for research. I agree to the following terms:

1. Research Project. These data will be submitted solely in connection with the "Research Project", specifically indicated and described in the Contributor Information and Certifications section.

Data submitted to NTRR may be made available by NTI and DoD for either collaborative research (i.e., to accelerate research on ongoing studies) or general research purposes (i.e., meta-analyses and other secondary uses of the data).

This Submission Agreement (SA) covers only the Research Project as contemplated in the Contributor Information and Certifications section. Contributor will submit a completed SA (this document) for each research project for which submission is requested.

2. Non-transferability of Agreement. This SA is not transferable. Contributing Investigator agrees that substantive changes the Contributing Investigator makes to the Research Project requires execution of a new SA, in which the new Research Project is designated. If the Contributing Investigator changes institutions and wishes to retain submission privileges to NTRR, a new SA in which the new institution acknowledges and agrees to the provisions of the SA is necessary.

3. Use of Common Data Elements. Contributing Investigator agrees to use the NTRR Common Data Elements as appropriate for their research. NTRR staff will work with researchers to map their study variables to specific CDEs.

4. Non-Identification of Subjects. Contributing Investigator agrees the data and/or images have been 'de-identified' according to the following criterion: the identities of subjects cannot be readily ascertained or otherwise associated with the data by the repository staff or secondary data users. Contributing Investigator further agrees not to disclose the identities of research participants to NTRR in the future and to verify that data and/or images lack identifiers after submission. Contributing Investigator agrees to notify NTRR as soon as possible if, upon review of NTRR data, the Contributing Investigator discovers identifying information in that data.

5. Data Disclaimers. Contributing Investigator agrees that DoD and NTI do not and cannot warrant the results that may be obtained by using any data or data analysis tools included in NTRR. DoD and NTI disclaim all warranties as to the accuracy of the data in NTRR or the performance or fitness of the data or data analysis tools for any particular purpose.

6. Supporting Materials. Contributing Investigator agrees to provide NTRR with supporting information and documentation ("Supporting Materials") to enable efficient use of the submitted data by investigators unfamiliar with the data. For example:
o Research protocol(s)
o Questionnaire(s)
o Study manuals
o Description of variables measures
o Other supporting documentation, as appropriate

7. Data Accuracy. Contributing Investigator certifies to the best of his/her knowledge and belief that the data submitted to NTRR are accurate. Contributing Investigator also agrees to perform the specified quality control activities within a timeframe specified by the NTRR Policy (see above). Contributing Investigator further agrees to notify NTRR as soon as possible if, upon review of NTRR data, the Contributing Investigator discovers data quality concerns.

8. Notification to DoD and NTI of Publication. Prompt publication or other public disclosure of the results of the Research Project is required. Contributing Investigator agrees to notify NTI as to when and where a publication (or other public disclosure) of a report from the Research Project will appear. Notification of such publications can occur by sending an email to research@nationaltraumainstitute.org with the title, authors, place of publication, and publication date. Notification of such publications can also occur by sending to NTRR an updated biographical sketch or CV of the publishing author.

9. Data Access for Research. Contributing Investigator agrees that data and Supporting Materials submitted to NTRR may be accessed and used broadly by qualified researchers for research and other activities as authorized by and consistent with law. This access may result in duplication of research data.

10. Non-Research Access. Contributing Investigator acknowledges that data and Supporting Materials submitted to NTRR become U.S. Government records that are subject to the Freedom of Information Act (FOIA). DoD and NTI are required to release Government records in response to (FOIA) requests unless they are exempt from release under one of the FOIA exemptions. Contributing Investigator further acknowledges that data and Submitting Materials may be used or released consistent with law.

11. Acknowledgments. In any and all publications based upon dataset(s) submitted to NTRR, Contributing Investigator agrees to cite NTRR, the relevant NTRR dataset identifier (a serial number), and the Contributing Investigators' federal research funding sources in each publication to which such datasets contribute (for abstracts, as space allows). The publication should include the following acknowledgement:

> Data used in the preparation of this article reside in the Department of Defense (DOD) and National Trauma Institute)-supported National Trauma Research Repository (NTRR) in [dataset identifier]. This manuscript reflects the views of the authors and does not reflect the opinions or views of the DOD or NTI.

Contributing Investigator agrees to acknowledge the contribution of the NTRR bioinformatics platform in any and all oral and written presentations, disclosures, and publications resulting from substantive analyses of data using NTRR tools. The manuscript should include the following acknowledgement:

Data and research tools used in the preparation of this article reside in and were analyzed using the Department of Defense (DOD) and National Trauma Institute (NTI)-supported National Trauma Research Repository (NTRR). NTRR is a collaborative biomedical repository created by DoD and NTI to provide a national resource to support and accelerate research of trauma. Dataset identifier: [provide]. This manuscript reflects the views of the authors and does not reflect the opinions or views of the DoD or NTI.

12. Non-Endorsement; Liability. Contributing Investigator agrees not to claim, infer, or imply endorsement by the United States Government, the Department of Defense, the Department of Health & Human Services, or the National Trauma Institute, the entity, or personnel conducting the Research Project or any resulting commercial product(s). The United States Government assumes no liability except to the extent provided under the Federal Tort Claims Act (28 U.S.C. § 2671-2680).

13. Contributing Investigator's Compliance with Institutional Requirements. Contributing Investigator acknowledges that these data were collected in a manner consistent with all applicable laws and regulations, as well as institutional policies. Contributing Investigator further acknowledges that the data were collected pursuant to an informed consent, if applicable, that is not inconsistent with the data submission, and that the data submitted were collected in accordance with applicable DHHS/FDA and DoD regulations, or applicable foreign law concerning the protection of human subjects, and other applicable U.S. federal and state laws, if any.

14. Contributing Investigator's Permission to Post Information Publicly. Contributing Investigator agrees to permit DoD and NTI to summarize and release for public use on the NTI Web site the Supporting Materials along with the Contributing Investigator's name and organizations/institutional affiliation.

15. Privacy Act Notification. The Contributing Investigator agrees that information collected from the Contributing Investigator, as part of the SA, may be made public in part or in whole for tracking and reporting purposes. This Privacy Act Notification is provided pursuant to Public Law 93-579, Privacy Act of 1974, 5 U.S.C. Section 552a. Authority for the collection of the information requested below from the Contributing Investigator comes from the authorities regarding the establishment of the National Trauma Institute's general authority to conduct and fund research and to provide training assistance, and its general authority to maintain records in connection with these and its other functions. These records will be maintained in accordance with the Privacy Act System of Records. The primary uses of this information are to document, track, monitor and evaluate the submission of data from clinical, basic, and population-based research activities and to notify Contributing Investigators in the event a potential error in the dataset is identified or in the event of updates or other changes to the database.

The Federal Privacy Act protects the confidentiality of the Contributing Investigator's NTI and DoD records. DoD and NTI will use the data collected for the purposes described above. In addition, the Act allows the release of some information in the Contributing Investigator's records without the Contributing Investigator's permission; for example, if it is required by members of Congress or other authorized individuals. The information requested is voluntary, but necessary for submitting data to NTRR.

16. Security. Contributing Investigator acknowledges the expectations set forth by the attached "NTRR Information Security Best Practices" for the use and security of data.

17. Amendments. Amendments to this SA must be made in writing and signed by authorized representatives of both parties.

18. Termination. Either party may terminate this SA without cause by providing 30 days written notice to the other party. NTRR will retain a copy of all data already submitted to NTRR for which data quality activities have been completed, except in the event that research participants withdraw consent for sharing of their data through the NTRR repository and DoD and NTI are informed by the Contributing Investigator to withdraw the data. Contributing Investigators agree to immediately report violations of NTRR Policy to the NTRR Steering Committee. Additionally, DoD and NTI may terminate this agreement with 5 days written notice if the agencies determine, in their sole discretion, that the Contributing Investigator has committed a material breach of this SA. The agencies may, in their

sole discretion, provide Contributing Investigator with 30 days' notice to remedy a breach before termination. Closed accounts may be reactivated upon submission of an updated Submission Request and SA.

19. One-Year Term and Access Period. Researchers who are granted permission to submit data to NTRR receive an account that is valid for a period of one year. This SA will automatically terminate at the end of one year. An account may be renewed upon recertification of a new SA. Accounts that remain inactive for 12 consecutive months may be closed at the discretion of DoD and NTI.

NTRR Information Security Best Practices

The purpose of these Security Best Practices, which are subject to applicable law, is to provide minimum security standards and best practices for individuals who use NTRR to submit, access, and analyze data. Keeping NTRR information secure through these best practices is important. Subject to applicable law, Contributing Investigators agree to immediately report breaches of data confidentiality to the NTRR Steering Committee.

Best Practices

• Do not attempt to override technical or management controls to access data for which you have not been expressly authorized.
• Do not use your trusted position and access rights to exploit system controls or access data for any reason other than in the performance of the proposed research.
• Ensure that anyone directed to use the system has access to, and is aware of, NTRR Information Security Best Practices and all existing policies and procedures relevant to the use of NTRR, including but not limited to, the NTRR policy.
• Follow the NTRR password policy which includes:
    • Choose passwords of at least seven characters including at least three of the following types of characters: capital letters, lower case letters, numeric characters and other special characters.
    • Change your passwords every six months.
    • Protect your NTRR password from access by other individuals—for example, store it electronically in a secure location.
    • Notify NTRR staff at research@nationaltraumainstitute.org of security incidents, or any incidents of suspected fraud, waste or misuse of NTRR or when access to NTRR is no longer required.

Security Standards
• Protect the data, providing access solely to authorized researchers permitted access to such data by your institution.
• Neither store nor transmit links between personally identifiable information and unique identifiers submitted with the data to NTRR.
• When you download NTRR data, download the data to a secured computer or server with strong password protection.
• For the computers hosting NTRR data, ensure that they have the latest security patches and are running virus protection software.
• Make sure the data are not exposed to the Internet or posted to a website that may be discovered by Internet search engines, such as Google or MSN.
• If you leave your office, close out of data files or lock your computer. Consider the installation of a timed screen saver with password protection.
• Avoid storing data on a laptop or other portable medium. If storing data on such a device, encrypt the data. Most operating systems have the ability to natively run an encrypted file system or encrypt portions of the file system (Windows = EFS or Pointsec and Mac OSX = File Vault).
• When finished using the data, destroy the data or otherwise dispose of them properly.

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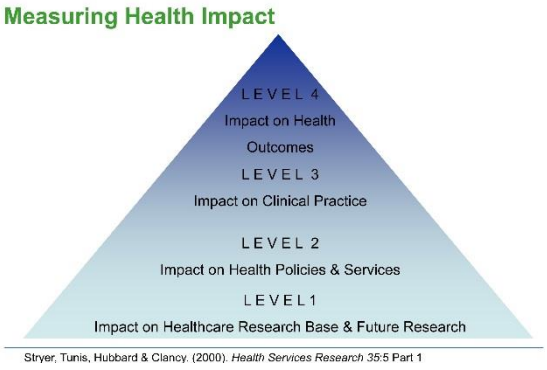
NTRR_Submission_R

NTI Knowledge Translation Plan→Moving Knowledge into Action

Knowledge translation: "Ensuring that stakeholders are aware of and use research evidence to inform their health and healthcare decision-making."

The private and public sectors together spend billions of dollars each year on biomedical, clinical and health services research; healthcare student and professional training; patient safety; and risk management. Despite this investment, healthcare systems still sometimes fail to deliver effective (or the most effective) treatments, services and drugs to all who need them, and health professionals may fail to provide the optimal level of care, as evidenced in studies. One of the most consistent findings from clinical and health services research is the failure to translate research into practice and policy. Evidence-practice gaps result in poorer health outcomes that can affect quality of life and productivity.

NTI's Knowledge Translation Plan transcends the traditional publication, presentation and—often years in process—public dissemination of data and results following scientific inquiry. This plan is in accordance with OSTP's 2013 policy memorandum calling for increased access to the results of federally funded scientific research. But because access is necessary but not sufficient to ensure knowledge translation (Ellen et al. cited in Grimshaw, 2012), NTI implements a robust, multi-media effort for access, dissemination, measurement, synthesis and translation that will result in new evidence-based practices that impact public health in a meaningful way. It seeks to be an effective learning system, as defined in the NASEM June 2017 report, one that supports "broad, rapid, meaningful change in practice."



The primary goals of this plan are to improve information flow to the trauma research community and enhance follow-on research; affect agency and government funding, policies and services; and enhance clinical practices. All goals are intended to affect the long-term intention, which is improved health outcomes for the traumatically injured, and enhanced public health overall.

A secondary goal is to identify translational research lags that can and should be decreased in order to shorten the time required for scientific inquiry to translate to new practices and improved outcomes. Knowledge translation barriers that contribute to lags include sheer volume, access, and lack of critical appraisal and research literacy skills. Further systemic barriers include financial and structural disincentives, peer group and professional issues, and difficulties working between and across professional health disciplines (Grimshaw, et al. Implementation Science 2012, 7:50, p. 6). NTI's Knowledge Translation Plan aims to overcome these barriers.

ACCESS

Access to research data will be achieved through research data and publication submissions to:

- Open source research libraries like ResearchGate
- Research data clearinghouses such as clinicaltrials.gov
- The National Trauma Research Repository (NTRR) and the National Trauma Data Base (NTDB)
- FITBIR and other topic-specific repositories, as appropriate

- Defense Technical Information Center (DTIC: www.dtic.mil). Because the Department of Defense provides much of the funding awarded to NTI research projects, NTI will interface with DTIC and, where appropriate, require researchers to submit their peer-reviewed, refereed manuscripts in final form to this repository in order to increase access. DTIC shares technical information related to funded studies with all DoD and affiliated industry and academic groups, provides collaboration tools, and performs research analyses. The DTIC's 12-month embargo ensures that manuscripts are published in scholarly journals before being made public. This powerful repository helps users monitor federally-funded research, identify research gaps, and forecast investment opportunities.
- Once a study is completed, its data will be uploaded into the National Trauma Research Repository (NTRR), now under construction. The NTRR will facilitate the sharing of information and yield long-term collective value. Aside from increased access to study data for researchers, a robust NTRR will result in increased visibility of research priorities and investment opportunities, avoidance of redundant research, and cost savings. It also meets the OSTP's guidance to increase public access to research results funded by the federal government.

DISSEMINATION

First, NTI expects that funded researchers will publish and present their findings in traditional high-impact venues including peer-reviewed journals and scientific conferences and other assemblies. New open-access journals such as *Trauma Surgery and Acute Care Open* and other publishing platforms like F1000Research provide high quality and speedier opportunities to disseminate research results, and NTI encourages funded researchers to publish in these forums as well.

In addition, primary investigators are encouraged to engage in less formal dissemination such as during grand rounds, lectures, department meetings and board presentations.

Following publication in peer-reviewed journals, primary investigators will submit a Publication Report form, which, in turn, signals NTI to activate its Dissemination Checklist. The checklist includes collaboration with the PI's institution on media, provision of a research summary to relevant medical organizations, announcements via NTI's contact list, posts to social media, and more.

NTI will disseminate research results in the popular, science, and health media using one or more technology-enabled platforms such as PRNewswire, AAAS EurekAlert!, and Meltwater. Individual dissemination efforts will encompass social media output on platforms such as Twitter and Facebook, with NTI connecting to all research funding recipients and amplifying their related posts. NTI is building a following among members of the trauma community, and will continue to add both depth and breadth within the follower base.

In order to provide the full range of functionality required of a research institution, NTI will construct a new state-of-the-art website. The NationalTraumaInstitution.org site will provide access and dissemination functionality, enabled by a flexible and searchable content management system to post and archive publications as they become available. The site's blog will be a forum for expert commentary on the archived work. In addition, the NationalTraumaInstitution.org website will host and moderate a robust community of interest surrounding trauma-related research, with multiple forums dedicated to the streams of research being explored. The website will also provide detailed information about the Trauma Clinical Trials Network to be tapped for the multi-institutional studies involved in the funded research, and about the participating clinical centers in any given study.

As new dissemination technologies and means of interaction and engagement emerge, NTI will grow to encompass them within its knowledge translation plan.

Already, NTI has a proven track record of dissemination—with 76% of NTI-funded studies resulting in one or more peer-reviewed publication(s) or manuscripts under review within two years. On average, only 29% of completed clinical trials have published within two years of study completion. (Chen R, Desai NR, Ross JS, Zhang W, Chau KH, Wayda B, Murugiah K, Lu, DY, Mittal A, Krumholz HM. Publication and reporting of clinical trials results: cross sectional analysis across academic medical centers. *BMJ*. 2016;352:i637).

MEASUREMENT

NTI expects its funded research to have a reach beyond the scholarly ecosystem, which means it must look beyond the Impact Factor (IF) and measure more than academic citations. IF has been the leading indicator of research impact since the 1950s. IF is a way to demonstrate research quality and impact, drawing on the data in the Web of Science (a subscription-based scientific citation indexing service used to calculate IF). In today's digital environment, however, IF has its limitations because it has become impossible, using this system of bibliometrics alone, to see the full picture of an article's impact. Alternate impact indicators are the Immediacy Index, calculating how soon after publication an article is cited, and the Cited Half-Life, which shows how often an article is referenced after being published, and there are others. None of them, however, accounts for alternative research outputs—they all rely on traditional scientific publication and conference presentation output.

Thus, NTI will combine traditional measures of scholarly impact with alternative metrics, as well as a variety of public relations measures such as PESO (paid, earned, shared, owned), to understand and quantify how research is being used in public policy and how scholars, practitioners and health agencies are viewing, saving, sharing and discussing research online. NTI will follow and analyze non-citation based, article-level indicators of impact—gathered from mentions of research in nontraditional online outlets. Such metrics will track research dissemination beyond academia; show attention, reception and response to a published work prior to its being cited; and apply to non-traditional research outputs like community forums, data-sets, and blog posts.

Every publication resulting from a NTI-funded study will be tagged with electronic retrieval information (i.e., Digital Object Identifier) to enable such enhanced tracking and analysis of reach and impact. NTI may need to become a member of a DOI Registration Agency such as DataCite or CrossRef if typical publishers of trauma-related research are not assigning DOIs.

SYNTHESIS, SUMMARY & TRANSLATION

Individual studies rarely provide sufficient evidence to support practice or policy changes—and in fact, can often be misleading. One of the most consistent findings from clinical and health services research is the failure to translate research into practice and policy. Research translation is complex and iterative: replication and evidence synthesis is needed before translation can occur (Grimshaw, 2012). NTI will facilitate this process with the development of a National Trauma Research Repository (NTRR), now under construction.

The NTRR will be the central repository for the clinical data resulting from both military and civilian federally funded trauma research and will be a free, web-based application with a user-friendly interface for trauma researchers to contribute and access data. The data-sharing enabled by the NTRR will reinforce open scientific inquiry, encourage diversity of analysis and opinion, more quickly bring to light research gaps, enable exploration of novel topics not envisioned by the initial investigators, and facilitate the education and engagement of new researchers. The NTRR will also facilitate knowledge translation between military and civilian researchers and care providers.

NTI will formally interface with the Eastern Association for the Surgery of Trauma (EAST) GRADES system for establishing Clinical Practice Guidelines and with American Association for the Surgery of Trauma (AAST) presentation and educational avenues such as webinars and scientific assemblies. It is through these established and respected channels that evidence-based practices emerge and become adopted within centers of care.

NTI will work with existing entities that undertake to review and synthesize research for the purpose of knowledge translation, including AHRQ Evidence-Based Practice Centers (EPCs - http://www.ahrq.gov/research/findings/evidence-based-reports/centers/index.html). NTI can nominate trauma treatment as a topic for analysis (AHRQ encourages topic nominations, weighting burden of disease and cost as important criteria. A quick search on "trauma" brought up just a handful of EPC reports, most on traumatic brain injury or injury related to violence, which indicates the agency has not already established trauma as a subject area for research synthesis, even though it is the third most costly medical condition, at $671 billion a year in health care costs and lost productivity, responsible for nearly 200,000 lives every year.) AHRQ has established EPCs at Brown University, the Mayo Clinic, Johns Hopkins, Oregon Health & Science University, Vanderbilt, and other hospital systems where NTI already has strong trauma center connections. Alternatively, or in addition, NTI may pursue establishment as an AHRQ EPC in order to be directly involved in the production of evidence reports related specifically to trauma-related care. Such reports are used for informing quality measures, educational materials and tools, clinical practice guidelines and research agendas.

Cochrane is another research synthesizer—an independent, global network of researchers, professionals, and care-givers—that seeks to improve health through informed, high-quality, relevant and up-to-date synthesized research evidence (http://www.cochrane.org/). Cochrane supports more than 50 review groups—including an anesthesia, critical and emergency care group (HQ in Denmark: http://ace.cochrane.org/) and an injuries group (HQ in London: http://injuries.cochrane.org/). NTI will pursue a partnership with Cochrane to insure that the knowledge translation process runs its full course.

ACCELERATING THE ADOPTION OF EVIDENCE-BASED PRACTICES

Morris et al. (J R Soc Med 2011:104:510-520) examined the literature related to the supposed 17-year gap in the conversion of basic science to patient benefit, determining that due to vast variations in what is measured, it's difficult to calculate an average. The conclusion is that research translation is complex and iterative, the type of research will affect the lag time to patient benefit, and a certain amount of lag is necessary and desired. The crucial questions to answer relate to identifying the specific contributions to lag (grant award process, ethical approvals process, publication and replication process, guideline preparation, and so forth) and which are beneficial or necessary and which unnecessary. Pinpointing the unnecessary gaps, and working to relieve those lags in the translation process will be a secondary goal of NTI's knowledge translation plan.

The National Trauma Institute has already undertaken an examination of gaps experienced by researchers it has funded, finding lags inherent in the regulatory approval process at one or more institutional levels, including IRB approval, DoD HRPO approval, the waiver of informed consent process, FDA approval, issues relating to multi-site and subcontracting. NTI will replicate this work with awarded studies in order to identify additional hurdles and tighten lags.

NTI's Knowledge Translation Plan identifies the key audiences to whom research knowledge will be transferred (researchers, policymakers and federal agencies, funders, practitioners/hospitals), how it will be transferred, the ways in which transference will be measured, and the practices and outcomes that are impacted (see attached spreadsheet).